10789403

File 5:Biosis Previews(R) 1926-2009/Dec W1
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Set	Items	Description
? s antennapedia and (chimer? or fusion)		
	848	ANTENNAPEDIA
	48374	CHIMER?
	123740	FUSION
S1	70	ANTENNAPEDIA AND (CHIMER? OR FUSION)

? t s1/7/40-70

1/7/40
DIALOG(R)File 5:Biosis Previews(R)

12632750 BIOSIS NO.: 199598100583
The C-terminus of the homeodomain is required for functional specificity of the Drosophila rough gene
AUTHOR: Heberlein Ulrike; Penton Andrea; Falsafi Sima; Hackett Davie; Rubin Gerald M
AUTHOR ADDRESS: Gallo Cent. Dep. Neurol., Build. 1, Room 101, Univ. Calfiornia San Francisco, San Francisco Gen. Hosp., San Francisco, CA 94110, USA**USA
JOURNAL: Mechanisms of Development 48 (1): p35-49 1994 1994
ISSN: 0925-4773
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In contrast to most Drosophila homeobox genes, which are required during embryogenesis, the rough gene is involved in photoreceptor cell specification in the compound eye. Taking advantage of the viability of null rough alleles and the small size of the rough gene, we have combined in vivo and in vitro mutagenesis to define important functional domains in the rough protein. All missense mutations found to disrupt rough function mapped to highly conserved amino acids in the homeodomain (HD), suggesting that the nature of few, if any, single amino acids outside the HD is critical for rough activity. The analysis of %%%chimeric%%% proteins, in which the whole HD or parts of it were swapped between the rough and %%%Antennapedia%%% (Antp) proteins, revealed that the C-terminus of the rough HD is important for rough activity in vivo. This C-terminal region was also found to be required for the recognition of rough binding sites in vitro. Our data suggest that amino acids located in the C-terminus of the homeodomain may play important roles in selective binding site recognition.

1/7/41
DIALOG(R)File 5:Biosis Previews(R)

12489341 BIOSIS NO.: 199497510626
Rab3A and Rab3B carboxy-terminal peptides are both potent and specific inhibitors of prolactin release by rat cultured anterior pituitary cells

AUTHOR: Perez Franck; Lledo Pierre-Marie; Karagogeos Domna; Vincent Jean-Didier (Reprint); Prochiantz Alain; Ayala Jesus
AUTHOR ADDRESS: CNRS UPR 2212, Inst. Alfred Fessard, 1 Ave. Terrasse, 91198 Gif sur Yvette Cedex, France**France
JOURNAL: Molecular Endocrinology 8 (9): p1278-1287 1994 1994
ISSN: 0888-8809
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%Chimeric%%% polypeptides composed of the homeodomain of %%%Antennapedia%%% and of the C-terminus of several low molecular weight GTP-binding proteins of the rab family have been found to translocate through the membrane of cells in culture and to accumulate in the cytoplasm and nucleus. We have used these %%%chimeric%%% peptides to study, in intact endocrine cells, a putative role for the C-terminal domain of rab proteins in the exocytotic process. We show that the internalization of 33- and 32-amino acid polypeptides corresponding to the C-terminal domains of rab3A and rab3B blocks calcium-triggered PRL release from adult rat anterior pituitary cells maintained in primary culture. This effect is specific to rab3 since it is not observed after internalization of either rab1 or rab2 C-terminal peptides. In addition, we demonstrate that this inhibition does not require the geranylgeranylation of the internalized C-termini. As rab3B normally shows a permissive effect on exocytosis in PRL-secreting cells, we suggest that the C-terminal domains of rab3A and rab3B contain structural elements that compete with endogeneous rab3 necessary for calcium-induced exocytosis.

1/7/42
DIALOG(R)File 5:Biosis Previews(R)

12475871 BIOSIS NO.: 199497497156
HOM-C/Hox genes and four interacting loci determine the morphogenetic properties of single cells in the nematode male tail
AUTHOR: Chow King L; Emmons Scott W (Reprint)
AUTHOR ADDRESS: Dep. Mol. Genetics, Albert Einstein Coll. Med., 1300 Morris Park Ave., Bronx, NY 10461, USA**USA
JOURNAL: Development (Cambridge) 120 (9): p2579-2592 1994 1994
ISSN: 0950-1991
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The copulatory structure of the C. elegans male tail includes a set of nine bilaterally symmetrical pairs of sense organs known as rays. Each ray comprises three cells, which are generated by a stereotyped cell sublineage expressed by 18 epidermal ray precursor cells. A pattern formation mechanism in the epidermis guides the specification of morphogenetic differences between the rays necessary for correct organelle assembly at specific positions within the epidermis. Expression of these ray differences was altered in mutations we described previously, resulting in displaced and fused rays. Here we show that two genes of the C elegans HOM-C/Hox gene complex play a role in the pattern formation mechanism. Increasing or decreasing the gene dosage of mab-5,

an %%%Antennapedia%%% homolog, and egl-5, an Abdominal B homolog, results in displacement and %%%fusion%%% of specific rays. These changes are interpreted as anterior or posterior transformations in ray identities. Mutations in the genes previously described are dominant modifiers of these effects. This suggests that these genes act in the same morphogenetic pathway as mab-5 and egl-5. Several lines of evidence, including cell ablation experiments, argue that the identity of each ray is specified cell-autonomously in the terminal cells of the ray lineages. mab-5 and egl-5, therefore, specify the morphogenetic properties of differentiating cells, without change in cell lineage or apparent cell type. Modifier genes may act upstream of mab-5 and egl-5 to regulate their expression. Alternatively, they may act at the same step in the pathway, as cofactors, or they may be target genes. Target genes could include genes specifying cell recognition and adhesion molecules governing ray organelle assembly.

1/7/43
DIALOG(R)File 5:Biosis Previews(R)

12396869 BIOSIS NO.: 199497418154
A differential response element for the homeotics at the %%%Antennapedia%%% P1 promoter of Drosophila
AUTHOR: Saffman Emma E; Krasnow Mark A (Reprint)
AUTHOR ADDRESS: Dep. Biochem., Stanford Univ., Stanford, CA 94305, USA**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 91 (16): p7420-7424 1994 1994
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Homeotic genes encode DNA-binding transcription factors that specify the identity of a segment or segments in particular body regions of Drosophila. The developmental specificity of these proteins results from their differential regulation of various target genes. This specificity could be achieved by use of different regulatory elements by the homeoproteins or by use of the same elements in different ways. The Ultrabithorax (UBX), abdominal-A (ABD-A), and %%%Antennapedia%%% (ANTP) homeoproteins differentially regulate the %%%Antennapedia%%% PI promoter in a cell culture cotransfection assay: UBX and ABD-A repress, whereas ANTP activates P1. Either of two regions of P1 can confer this pattern of differential regulation. One of the regions lies downstream and contains homeoprotein-binding sites flanking a 37-bp region called BetBS. ANTP protein activates transcription through the binding sites, whereas UBX and ABD-A both activate transcription through BetBS and use the flanking binding sites to prevent this effect. Thus, homeoproteins can use the same regulatory element but in very different ways. %%%Chimeric%%% UBX-ANTP proteins and UBX deletion derivatives demonstrate that functional specificity in P1 regulation is dictated mainly by sequences outside the homeodomain, with important determinants in the N-terminal region of the proteins.

1/7/44
DIALOG(R)File 5:Biosis Previews(R)

11971525 BIOSIS NO.: 199396135941
Binding of a phosphoprotein to the 3' untranslated region of the mouse protamine 2 mRNA temporally represses its translation
AUTHOR: Kwon Yunhee Kim; Hecht Norman B (Reprint)
AUTHOR ADDRESS: Dep. Biol., Tufts University, Medford, MA 02155, USA**USA
JOURNAL: Molecular and Cellular Biology 13 (10): p6547-6557 1993
ISSN: 0270-7306
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The synthesis of the protamines, the predominant nuclear proteins of mammalian spermatozoa, is regulated during germ cell development by mRNA storage for about 7 days in the cytoplasm of differentiating spermatids. Two highly conserved sequences, the Y and H elements present in the 3' untranslated regions (UTRs) of all known mammalian protamine mRNAs, form RNA-protein complexes and specifically bind a protein of 18 kDa. Here, we show that translation of %%%fusion%%% mRNAs was markedly repressed in reticulocyte lysates supplemented with a mouse testis extract enriched for the 18-kDa protein when the mRNAs contained the 3' UTR of mouse protamine 2 (mP2) or the Y and H elements of mP2. No significant decrease was seen when the %%%fusion%%% mRNAs contained the 3' UTR of human growth hormone. The 18-kDa protein is developmentally regulated in male germ cells, requires phosphorylation for RNA binding, and is found in the ribonucleoprotein particle fractions of a testicular postmitochondrial supernatant. We propose that a phosphorylated 18-kDa protein plays a primary role in repressing translation of mP2 mRNA by interaction with the highly conserved Y and H elements. At a later stage of male gamete differentiation, the 18-kDa protein no longer binds to the mRNA, likely as a result of dephosphorylation, enabling the protamine mRNA to be translated.

1/7/45
DIALOG(R)File 5:Biosis Previews(R)

11948177 BIOSIS NO.: 199396112593
Abdominal-B protein isoforms exhibit distinct cuticular transformations and regulatory activities when ectopically expressed in Drosophila embryos
AUTHOR: Kuziora Michael A
AUTHOR ADDRESS: Dep. Biol. Sci., Univ. Pittsburgh, A234 Langley Hall, Pittsburgh, PA 15260, USA**USA
JOURNAL: Mechanisms of Development 42 (3): p125-137 1993
ISSN: 0925-4773
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The Drosophila homeotic gene Abdominal-B includes two genetically distinct elements, a morphogenetic (m) activity and a regulatory (r) activity. The proteins responsible for these activities were ectopically expressed in fly embryos. The larval cuticular transformations which result are consistent with the genetically defined role of each protein during normal embryogenesis. Both ABD-B proteins activate ectopic

expression of transcripts encoding the m protein, but the levels of %%%Antennapedia%%%, Ultrabithorax and abdominal-A transcripts are differentially repressed. A structural and functional comparison of the ABD-B proteins and a %%%chimeric%%% DFD/ABD-B protein reaffirms that target specificity is largely determined by the homeodomain region and suggests protein domains outside of the homeodomain influence the activation or repression of target gene expression.

1/7/46
DIALOG(R)File 5:Biosis Previews(R)

11898840 BIOSIS NO.: 199396063256
Functional specificity of the %%%antennapedia%%% homeodomain
AUTHOR: Furukubo-Tokunaga Katsuo (Reprint); Flister Susanne; Gehring Walter J
AUTHOR ADDRESS: Dep. Neurobiology, Zoologisccches Inst., Univ. Basel, Rheinsprung 9, CH-4051 Basel, Switzerland**Switzerland
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 90 (13): p6360-6364 1993
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The segmental identity in animal development is determined by a set of homeotic selector genes clustered in the invertebrate HOM or vertebrate Hox homeo box complexes. These genes encode proteins with very similar homeodomains and highly diverged N- and C-terminal sequences. The %%%Antennapedia%%% (Antp) homeodomain, for instance, differs at only five amino acid positions from that of Sex combs reduced (Scr) protein. Using a heat shock assay in which %%%chimeric%%% Antp-Scr proteins are expressed ectopically in Drosophila, we have shown that the functional specificity of the Antp protein is determined by the four specific amino acids located in the flexible N-terminal arm of the homeodomain. The three-dimensional structure of the Antp homeodomain-DNA complex shows that this N-terminal arm is located in the minor groove of the DNA, suggesting that the functional specificity is determined either by slight differences in DNA binding and/or by selective interactions with other transcription factor(s).

1/7/47
DIALOG(R)File 5:Biosis Previews(R)

11898637 BIOSIS NO.: 199396063053
Ectopic expression and function of the Antp and Scr homeotic genes: The N-terminus of the homeodomain is critical to functional specificity
AUTHOR: Zeng Wenlin; Andrew Deborah J; Mathies Laura; Horner Michael A; Scott Matthew P (Reprint)
AUTHOR ADDRESS: Dep. Dev. Biol. and Genetics, Stanford Univ. Sch. Med., Stanford, CA 94305-5427, USA**USA
JOURNAL: Development (Cambridge) 118 (2): p339-352 1993
ISSN: 0950-1991
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The transcription factors encoded by homeotic genes determine cell fates during development. Each homeotic protein causes cells to follow a distinct pathway, presumably by differentially regulating downstream 'target' genes. The homeodomain, the DNA-binding part of homeotic proteins, is necessary for conferring the specificity of each homeotic protein's action. The two Drosophila homeotic proteins encoded by %%%Antennapedia%%% and Sex combs reduced determine cell fates in the epidermis and internal issues of the posterior head and thorax. Genes encoding %%%chimeric%%% Antp/Scr proteins were introduced into flies and their effects on morphology and target gene regulation observed. We find that the N terminus of the homeodomain is critical for determining the specific effects of these homeotic proteins in vivo, but other parts of the proteins have some influence as well. The N-terminal part of the homeodomain has been observed, in crystal structures and in NMR studies in solution, to contact the minor groove of the DNA. The different effects of %%%Antennapedia%%% and Sex combs reduced proteins in vivo may depend on differences in DNA binding, protein-protein interactions, or both.

1/7/48
DIALOG(R)File 5:Biosis Previews(R)

11817762 BIOSIS NO.: 199395120028
In vitro binding to the leucine tRNA gene identifies a novel yeast homeobox gene
AUTHOR: Kaufmann Eckhard
AUTHOR ADDRESS: Max-Planck-Inst. biophysikalische Chem., Abt. Mol. Entwicklungsbiol., Am Fassberg, W-3400 Goettingen 23, Germany**Germany
JOURNAL: Chromosoma (Berlin) 102 (3): p174-179 1993
ISSN: 0009-5915
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In a search for gene products of Saccharomyces cerevisiae interacting with the internal promoter of yeast tRNA genes two genes encoding a homeodomain protein of the Drosophila %%%Antennapedia%%% type were isolated. One of them codes for Pho2, and the second codes for a previously unknown protein (Yox1). The corresponding gene, termed YOX1, maps to chromosome 16. The amino acid sequence of Yox1 shows a remarkable similarity within the homeobox domain to many proteins from a wide variety of sources. %%%Fusion%%% proteins that contain sequences encoded by these genes demonstrate that the genes encode DNA-binding proteins that are capable of binding to the DNA of the leucine tRNA gene in vitro. However, deletion of YOX1 gene activity does not give rise to a scorable mutant phenotype. This result leaves open whether Yox1 binding to the leucine tRNA gene is necessary for the in vivo regulation of the gene and its suggests that the YOX1 gene codes for a nonessential product.

1/7/49
DIALOG(R)File 5:Biosis Previews(R)

11759340 BIOSIS NO.: 199395061606
POU-specific domain of Oct-2 factor confers "octamer" motif DNA binding specificity on heterologous %%%Antennapedia%%% homeodomain
AUTHOR: Brugnera Enrico; Xu Licen; Schaffner Walter; Arnosti David N
AUTHOR ADDRESS: Inst. Molecular Biol. II, Univ. Zurich, Winterthurerstrasse 190, CH-8057 Zurich, Switzerland**Switzerland
JOURNAL: FEBS (Federation of European Biochemical Societies) Letters 314 (3): p361-365 1992
ISSN: 0014-5793
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The bipartite DNA binding domain of the POU family of transcription factors contains a 'POU-specific' domain unique to this class of factors and a 'POU homeodomain' homologous to other homeodomains. We compared DNA binding of the Oct-2 factor POU domain and the %%%Antennapedia%%% (Antp) homeodomain with a %%%chimeric%%% Oct-2/Antp protein in which the distantly related Antp homeodomain was substituted for the Oct-2 POU homeodomain. The Oct-2/Antp %%%chimeric%%% protein bound both the octamer and the Antp sites efficiently, indicating that DNA binding specificity is contributed by both components of the POU domain.

1/7/50
DIALOG(R)File 5:Biosis Previews(R)

11737450 BIOSIS NO.: 199395039716
Expression of the homeotic gene mab-5 during Caenorhabditis elegans embryogenesis
AUTHOR: Cowing Deborah W; Kenyon Cynthia
AUTHOR ADDRESS: Dep. Biochemistry Biophysics, Univ. California, San Francisco, Calif. 94143-0554, USA**USA
JOURNAL: Development (Cambridge) 116 (2): p481-490 1992
ISSN: 0950-1991
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: mab-5 is a member of a complex of homeobox-containing genes evolutionarily related to the %%%antennapedia%%% and bithorax complexes of Drosophila melanogaster. Like the homeotic genes in Drosophila, mab-5 is required in a particular region along the anterior-posterior body axis, and acts during postembryonic development to give cells in this region their characteristic identities. We have used a mab-5-lacZ %%%fusion%%% integrated into the C. elegans genome to study the posterior-specific expression of mab-5 during embryogenesis. The mab-5-lacZ %%%fusion%%% was expressed in the posterior of the embryo by 180 minutes after the first cleavage, indicating that the mechanisms responsible for the position-specific expression of mab-5-lacZ act at a relatively early stage of embryogenesis. In embryos homozygous for mutations in the par genes, which disrupt segregation of factors during early cleavages, expression of mab-5-lacZ was no longer localized to the

posterior. This suggests that posterior-specific expression of mab-5 depends on the appropriate segregation of developmental factors during early embryogenesis. After extrusion of any blastomere of the four-cell embryo, descendants of the remaining three cells could still express the mab-5-lacZ %%%fusion%%%. In these partial embryos, however, the %%%fusion%%% was often expressed in cells scattered throughout the embryo, suggesting that cell-cell interactions and/or proper positioning of early blastomeres are required for mab-5 expression to be localized to the posterior.

1/7/51
DIALOG(R)File 5:Biosis Previews(R)

11430699 BIOSIS NO.: 199294132540
%%%ANTENNAPEDIA%%% HOMEOBOX AS A SIGNAL FOR THE CELLULAR INTERNALIZATION AND NUCLEAR ADDRESSING OF A SMALL EXOGENOUS PEPTIDE
AUTHOR: PEREZ F (Reprint); JOLIOT A; BLOCH-GALLEGO E; ZAHRAOUI A; TRILLER A ; PROCHIANTZ A
AUTHOR ADDRESS: CNRS URA 1414, ECOLE NORMALE SUPERIEURE, 46 RUE D'ULM, 75230 PARIS CEDEX 05, FR**FRANCE
JOURNAL: Journal of Cell Science 102 (4): p717-722 1992
ISSN: 0021-9533
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: In a previous study we demonstrated that a homeobox peptide corresponding to the 60 amino acid long DNA-binding region of the Drosophila %%%antennapedia%%% homeoprotein was capable of crossing the plasma membrane of cells in culture. This finding has led us to investigate whether %%%chimeric%%% molecules encompassing the homeobox would behave in a similar manner. We demonstrate here that a peptide of 93 amino acids composed of the homeobox and of the C terminus of Rab3, a small GTP-binding protein, crosses the membrane of myoblasts, myotubes and neurons and is conveyed to their nuclei. This transport is highly efficient, is observed in all the cells present in the culture and occurs at 37.degree. C and 12.degree. C without quantitative peptide degradation. Beyond its theoretical implications for our current views on cellular interactions, this finding could have technical repercussions on the development of drugs with intracellular targets.

1/7/52
DIALOG(R)File 5:Biosis Previews(R)

11406312 BIOSIS NO.: 199294108153
AT-RICH PROMOTER ELEMENTS OF SOYBEAN HEAT SHOCK GENE GMHSP17.5E BIND TWO DISTINCT SETS OF NUCLEAR PROTEINS IN-VITRO
AUTHOR: CZARNECKA E (Reprint); INGERSOLL J C; GURLEY W B
AUTHOR ADDRESS: DEP MICROBIOLOGY CELL SCIENCE, 3103 MCCARTY HALL, UNIVERSITY FLORIDA, GAINESVILLE, FLA 32611-0100, USA**USA
JOURNAL: Plant Molecular Biology 19 (6): p985-1000 1992
ISSN: 0167-4412
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A 33 bp double-stranded oligonucleotide homologous to two AT-rich sequences located upstream (-907 to -889 and -843 to -826) to the start of transcription of heat shock gene Gmhsp17.5E of soybean stimulated transcriptions when placed 5' to a truncated (-140) maize Adh1 promoter. The %%%chimeric%%% promoter was assayed in vivo utilizing anaerobically stressed sunflower tumors transformed by a pTi-based vector of Agrobacterium tumefaciens. Nuclear proteins extracted from soybean plumules were shown to bind double-stranded oligonucleotides homologous to AT-rich sequences in the 5' flanking regions of soybean .beta.-conglycinin, lectin, leghemoglobin and heat shock genes. These proteins were also shown to bind AT-rich probes homologous to homeobox protein binding sites from the %%%Antennapedia%%% and engrailed/fushi tarazu genes of Drosophila. Binding activity specific for AT-rich sequences showed a wide distribution among various plant organs and species. Preliminary characterization indicated that two sets of nuclear proteins from soybean bind AT-rich DNA sequences: a diverse high-molecular-weight (ca. 46-69 kDa) group, and a low-molecular-weight (23 and 32 kDa) group of proteins. The latter meets the operational criteria for high-mobility group proteins (HMGs).

1/7/53
DIALOG(R)File 5:Biosis Previews(R)

11348658 BIOSIS NO.: 199294050499
IN-VIVO ANALYSIS OF THE HELIX-TURN-HELIX MOTIF OF THE FUSHI TARAZU HOMEO DOMAIN OF DROSOPHILA-MELANOGASTER
AUTHOR: FURUKUBO-TOKUNAGA K (Reprint); MULLER M; AFFOLTER M; PICK L; KLOTER U; GEHRING W J
AUTHOR ADDRESS: DEP CELL BIOLOGY, BIOZENTRUM, UNIV BASEL, CH-4056 BASEL, SWITZ**SWITZERLAND
JOURNAL: Genes and Development 6 (6): p1082-1096 1992
ISSN: 0890-9369
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We report a systemic mutational analysis of the helix-turn-helix motif (HTH) of the fushi tarazu (ftz) homeo domain (HD) of Drosophila. We started out by testing the function of %%%chimeric%%% ftz proteins containing either a part of the Sex combs reduced (Scr) or the muscle segment homeobox (msh) HDs. By complementation tests in transgenic flies, cotransfection assays in cultured Drosophila cells and in vitro DNA-binding assays, we have found that the ftz activity is retained in the ftz-Scr %%%chimera%%% but is lost in the ftz-msh %%%chimera%%%, which is defective in binding to an %%%Antennapedia%%% (Antp)-class target site. Further studies with a series of back-mutants of the ftz-msh %%%chimera%%% have revealed that a set of class-specific DNA backbone-contacting residues in the HTH, particularly Arg-28 and Arg-43, are required for efficient target site recognition and, hence, full ftz activity both in vitro and in vivo.

1/7/54
DIALOG(R)File 5:Biosis Previews(R)

11348657 BIOSIS NO.: 199294050498
MAPPING FUNCTIONAL SPECIFICITY IN THE DFD AND UBX HOMEO DOMAINS
AUTHOR: LIN L (Reprint); MCGINNIS W
AUTHOR ADDRESS: DEP MOLECULAR BIOPHYSICS BIOCHEMISTRY, YALE UNIV, NEW HAVEN, CONN 06511, USA**USA
JOURNAL: Genes and Development 6 (6): p1071-1081 1992
ISSN: 0890-9369
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: To define homeo domain subregions that are important for embryonic targeting specificity of homeotic proteins, we generated a series of Deformed/Ultrabithorax %%%chimeric%%% genes in which parts of the Deformed homeo box region were substituted with Ultrabithorax sequences. %%%Chimeric%%% coding regions were attached to heat shock promoters and introduced into the Drosophila genome by P-element transformation. After heat-induced ectopic expression in embryos, we examined the cuticular phenotypes induced by the resulting %%%chimeric%%% proteins. We also tested the ability of the %%%chimeric%%% proteins to regulate transcription units that are normal targets of Deformed and Ultrabithorax. Our results indicate that specific amino acid residues at the amino end of the Ultrabithorax homeo domain are required to specifically regulate %%%Antennapedia%%% transcription; and in the context of a Deformed protein, these amino-end residues are sufficient to switch from Deformed- to Ultrabithorax-like targeting specificity. Although residues in the amino end of the homeo domain are also important in determining a Deformed-like targeting specificity, other regions of the Deformed homeo domain are also required for full activity.

1/7/55
DIALOG(R)File 5:Biosis Previews(R)

11315978 BIOSIS NO.: 199294017819
SPATIAL AND TEMPORAL EXPRESSION OF AN %%%ANTENNAPEDIA%%%-LAC Z GENE CONSTRUCT INTEGRATED INTO THE ENDOGENOUS %%%ANTENNAPEDIA%%% GENE OF DROSOPHILA-MELANOGASTER
AUTHOR: ENGSTROEM Y (Reprint); SCHNEUWLY S; GEHRING W J
AUTHOR ADDRESS: DEP MOL BIOL, UNIV STOCKHOLM, S-106 91 91 STOCKHOLM, SWED** SWEDEN
JOURNAL: Roux's Archives of Developmental Biology 201 (2): p65-80 1992
ISSN: 0930-035X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: In order to study the regulation of spatial and temporal expression of the homeotic gene %%%Antennapedia%%% (Antp) in Drosophila melanogaster, we have constructed %%%fusion%%% genes which contain Antp sequences linked to the reporter gene lac Z of Escherichia coli. In one case of P-element transformation, a %%%fusion%%% gene construct

integrated into the endogenous Antp gene close to one of the two promoters (P1). The spatial expression from the reporter gene in this transformant line, as analysed by the detection of .beta.-galactosidease activity, was found to exactly mimic the normal expression from the P1 promoter of the Antp gene. We have used this unique transformant as a tool for studying the expression of the P1 promoter in embryonic, larval and adult development. Parallel lines transformed with the same %%%fusion%%% gene construct did not confer a correct P1 patterns of expression. The position in the genome was, therefore, crucial for the expression pattern of the reporter gene. Experiments aiming at the detection of autoregulatory control of Antp gene expression were designed. The results did not, however, support models of positive or negative autoregulation of P1 expression by Antp protein.

1/7/56

11222643 BIOSIS NO.: 199293065534
IDENTIFICATION OF TARGET GENES OF THE HOMEOTIC GENE %%%ANTENNAPEDIA%%% BY ENHANCER DETECTION
AUTHOR: WAGNER-BERNHOLZ J T (Reprint); WILSON C; GIBSON G; SCHUH R; GEHRING W J
AUTHOR ADDRESS: BIOZENTRUM, UNIV BASEL, CH-4056 BASEL, SWITZ**SWITZERLAND
JOURNAL: Genes and Development 5 (12B): p2467-2480 1991
ISSN: 0890-9369
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Localized expression of the homeotic gene %%%Antennapedia%%% (Antp) in Drosophila melanogaster is required for normal development of the thoracic segments. When the Antp gene is expressed ectopically in the larval primordium of the antenna, the antennal imaginal disc, the developmental fate of the disc is switched and the adult antenna is tranformed to a mesothoracic leg. We screened .apprx.550 different fly strains carrying single copies of an enhancer-detector transposon to identify regulatory elements and corresponding genes that are either activated or repressed in antennal discs in response to this transformation. Several regulatory elements that are either direct or indirect targets of Antp were found. One transposant that expresses the reporter gene (lacZ) in the antennal disc, but not in the leg disc, was studied in more detail. The enhancer detector in this strain is located near a similarly regulated gene at the spalt (sal) locus, which encodes a homeotic function involved in embryonic head and tail development. The expression of this newly discovered gene, spalt major (salm) is strongly repressed in gain-of-function mutants that express Antp in the antennal disc. Recessive loss-of-function mutations (Antp-) have the opposite developmental effect; they cause the differentiation of antennal structures in the second leg disc. Accordingly, salm is derepressed in clones of homozygous Antp- cells. Therefore, we conclude that Antp negatively regulates salm. The time course of the interaction and reporter gene %%%fusion%%% experiments suggests (but does not prove) a direct interaction between Antp and cis-regulatory elements of salm. Our analysis of several enhancer-detector strains suggests that the basic patterning information in the antennal and leg imaginal discs is very

similar.

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DIALOG(R)File 5:Biosis Previews(R)

10853672 BIOSIS NO.: 199192099443
A HOMEODOMAIN PROTEIN BINDS TO GAMMA GLOBIN GENE REGULATORY SEQUENCES
AUTHOR: LAVELLE D (Reprint); DUCKSWORTH J; EVES E; GOMES G; KELLER M; HELLER P; DESIMONE J
AUTHOR ADDRESS: DEP MED, UNIV ILLINOIS AT CHICAGO, VETERANS ADMINISTRATION WESTSIDE MED CENTER, CHICAGO, ILL 60612, USA**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 88 (16): p7318-7322 1991
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Developmental regulation of .gamma.-globin gene expression probably occurs through developmental-stage-specific trans-acting factors able to promote the interaction of enhancer elements located in the far upstream locus control region with regulatory elements in the .gamma. gene promoters and 3' A.gamma. enhancer located in close proximity to the genes. We have detected a nuclear protein in K562 and baboon fetal bone marrow nuclear extracts capable of binding to A+T-rich sequences in the locus control region, .gamma. gene promoter, and 3' A.gamma. enhancer. SDS/polyacrylamide gel analysis of the purified K562 binding activity revealed a single protein of 87 kDa. A K562 cDNA clone was isolated encoding a .beta.-galactosidase %%%fusion%%% protein with a DNA binding specificity identical to that of the K562/fetal bone marrow nuclear protein. The cDNA clone encodes a homeodomain homologous to the Drosophila %%%antennapedia%%% protein.

1/7/58
DIALOG(R)File 5:Biosis Previews(R)

10645163 BIOSIS NO.: 199191028054
THE DNA BINDING SPECIFICITY OF THE DROSOPHILA FUSHI TARAZU PROTEIN A POSSIBLE ROLE FOR DNA BENDING IN HOMEODOMAIN RECOGNITION
AUTHOR: NELSON H B (Reprint); LAUGHON A
AUTHOR ADDRESS: LAB GENETICS, UNIV WIS-MADISON, MADISON, WIS 53706, USA** USA
JOURNAL: New Biologist 2 (2): p171-178 1990
ISSN: 1043-4674
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Segmentation in Drosophila melanogaster is controlled by a network of interacting genes, many of which encode a homeodomain that confers sequence-specific binding to DNA. One of these, fushi tarazu (ftz), is a transcription factor that regulates a number of segmentation and homeotic genes, including %%%Antennapedia%%% (Antp). To determine the

DNA binding specificity of the ftz homeodomain, we performed DNase I footprint analysis on ftz protein binding sites located near the two Antp promoters using a .beta.-galactoside/ftz %%%fusion%%% protein synthesized in E. coli. A consensus sequence for the %%%fusion%%% protein's preferred binding site was derived from 19 sites. The consensus sequence contains an ATTA motif, as do the reported consensus sequences for the engrailed (en), even-skipped (eve), and bicoid (bcd) Drosophila homeodomain proteins. We propose DNA bending as an explanation for the presence of a shared motif between proteins with divergent recognition helices: according to this model, bases in ATTA would not directly contact amino acid side chains of the recognition helix but rather would be necessary for bending of the DNA around the homeodomain, perhaps facilitating important protein-DNA contacts.

1/7/59
DIALOG(R)File 5:Biosis Previews(R)

10187356 BIOSIS NO.: 199089105247
FUNCTIONAL DISSECTION OF ULTRABITHORAX PROTEINS IN DROSOPHILA-MELANOGASTER
AUTHOR: MANN R S (Reprint); HOGNESS D S
AUTHOR ADDRESS: DEP BIOCHEM, BECKMAN CENT, STANFORD UNIV SCH MED, STANFORD, CALIF 94305, USA**USA
JOURNAL: Cell 60 (4): p597-610 1990
ISSN: 0092-8674
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Expression of Ultrabithorax (UBX) proteins via a heat-inducible promoter generated homeotic transformations of segmental identities in the embryonic cuticle and peripheral nervous system (PNS) of Drosophila and transformed antennae into legs in the adult. The embryonic transformations were used to determine the identity functions of members of the UBX family and UBX mutant forms. Whereas UBX forms I and IV each induced the cuticle transformations, only form I induced the PNS transformations. Analysis of the transformations generated by UBX deletions and by a %%%chimeric%%% Ultrabithorax-%%%Antennapedia%%% protein demonstrated that the majority of the UBX identity information is contained within the C-terminal, homeodomain-containing portion of the protein. Implications of these results for how homeotic proteins select particular metameric identities are discussed.

1/7/60
DIALOG(R)File 5:Biosis Previews(R)

10107203 BIOSIS NO.: 199089025094
A HOMEODOMAIN SUBSTITUTION CHANGES THE REGULATORY SPECIFICITY OF THE DEFORMED PROTEIN IN DROSOPHILA EMBRYOS
AUTHOR: KUZIORA M A (Reprint); MCGINNIS W
AUTHOR ADDRESS: DEP MOL BIOPHYS BIOCHEM, YALE UNIV, NEW HAVEN, CONN 06511, USA**USA
JOURNAL: Cell 59 (3): p563-572 1989
ISSN: 0092-8674

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Homeodomain proteins are believed to direct developmental pathways during Drosophila embryogenesis by the specific regulation of other genes. An unresolved issue is whether it is the homeodomain or the other regions of such proteins that confer target specificity. To test the role of the homoeodomain in determining target specificity, we replaced the homeobox of Deformed with the homeobox of Ultrabithorax. The resulting %%%chimeric%%% protein cannot activate transcription from the Deformed gene, as does the normal Deformed protein. Instead, the %%%chimeric%%% protein activates ectopic transcription of %%%Antennapedia%%%, a gene normally regulated by Ultrabithorax. Our results indicate that in the context of the developing embryo, even closely related homeodomain sequences have different target specificities.

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DIALOG(R)File 5:Biosis Previews(R)

09758408 BIOSIS NO.: 198988073523
DNA SPECIFICITY OF THE BICOID ACTIVATOR PROTEIN IS DETERMINED BY HOMEODOMAIN RECOGNITION HELIX RESIDUE 9
AUTHOR: HANES S D (Reprint); BRENT R
AUTHOR ADDRESS: DEP MOL BIOL, MASSACHUSETTS GENERAL HOSP, BOSTON, MASS 02114, USA**USA
JOURNAL: Cell 57 (7): p1275-1283 1989
ISSN: 0092-8674
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Formation of anterior structures in the Drosophila embryo requires the product of the gene bicoid. The bicoid protein contains a homeodomain and may exert its effects in early development by regulating transcription of the gap gene, hunchback (hb). Consistent with this view, we have demonstrated that DNA-bound Bicoid %%%fusion%%% proteins stimulate gene expression. We used the gene activation phenotype in yeast to study DNA recognition by the Bicoid homeodomain. We found that a single amino acid replacement at position 9 of the recognition helix was sufficient to switch the DNA specificity of the Bicoid protein. The altered specificity Bicoid mutants recognized DNA sites bound by Ultrabithorax, fushi tarazu, and other related homeodomain proteins. Our results suggest that DNA specificity in Bicoid and %%%Antennapedia%%% class proteins is determined by recognition helix residue 9.

1/7/62
DIALOG(R)File 5:Biosis Previews(R)

09746295 BIOSIS NO.: 198988061410
TRANSCRIPTIONAL ACTIVATION AND REPRESSION BY ULTRABITHORAX PROTEINS IN CULTURED DROSOPHILA CELLS

AUTHOR: KRASNOW M A (Reprint); SAFFMAN E E; KORNFELD K; HOGNESS D S
AUTHOR ADDRESS: DEP BIOCHEM, STANFORD UNIV, STANFORD, CALIF 94305, USA**USA
JOURNAL: Cell 57 (6): p1031-1044 1989
ISSN: 0092-8674
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Homeotic genes of Drosophila melanogaster such as Ultrabithorax (Ubx) and %%%Antennapedia%%% (Antp) have long been thought to select metameric identify during development by controlling the expression of various target genes. Here we describe a cotransfection assay in cultured D. melanogaster cells that is used to demonstrate that Ubx proteins (UBX) can repress an Antp promoter %%%fusion%%% and activate a Ubx promoter %%%fusion%%%, activities predicted from genetic studies. We show (a) that UBX proteins regulated the level of accurately initiated Antp P1 and Ubx transcripts, (b) that activation of the Ubx promoter required a downstream cluster of UBX binding sites, and (c) that binding site sequences were sufficient to confer regulation on a heterologous promoter, regardless of their orientation or precise position. We conclude that UBX proteins are transcriptional repressors and activators, and that their actions are mediated by binding to promoter region sequences. Each member of the UBX protein family has similar regulatory abilities, but the properties of synthetic mutant forms suggest that UBX proteins may have a modular design similar to other transcriptional regulators.

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DIALOG(R)File 5:Biosis Previews(R)

09708928 BIOSIS NO.: 198988024043
XLHBOX 8 A NOVEL XENOPUS HOMEO PROTEIN RESTRICTED TO A NARROW BAND OF ENDODERM
AUTHOR: WRIGHT C V E (Reprint); SCHNEGELSBERG P; DE ROBERTIS E M
AUTHOR ADDRESS: DEP BIOLOGICAL CHEM, UNIV CALIF, LOS ANGELES, CALIF 90024-1737, USA**USA
JOURNAL: Development (Cambridge) 105 (4): p787-794 1989
ISSN: 0950-1991
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: We report the isolation of a new homeobox gene from Xenopus laevis genomic DNA. The homeodomain sequence is highly diverged from the prototype %%%Antennapedia%%% sequence, and contains a unique histidine residue in the helix that binds to DNA. The homeodomain is followed by a 65 amino acid carboxy-terminal domain, the longest found to date in any vertebrate homeobox gene. We have raised specific antibodies against an XIHbox 8-.beta.-gal %%%fusion%%% protein to determine the spatial and temporal expression of this gene. The nuclear protein first appears in a narrow band of the endoderm at stage 33 and develops into expression within the epithelial cells of the pancreatic anlagen and duodenum. Expression within the pancreatic epithelium persists into the adult frog. This unprecedented restriction to an anteroposterior band of the endoderm suggests that vertebrate homeobox genes might be involved in specifying

positional information not only in the neuroectoderm and mesoderm, but also in the endoderm. Our data suggest tht XIHbox 8 may therefore represent the first member of a new class of position-dependent transcription factors affecting endodermal differentiation.

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DIALOG(R)File 5:Biosis Previews(R)

09677637 BIOSIS NO.: 198987125528
ISOLATION STRUCTURE AND EXPRESSION OF LABIAL A HOMEOTIC GENE OF THE %%%ANTENNAPEDIA%%% COMPLEX INVOLVED IN DROSOPHILA HEAD DEVELOPMENT
AUTHOR: DIEDERICH R J (Reprint); MERRILL V K L; PULTZ M A; KAUFMAN T C
AUTHOR ADDRESS: MOL CELL DEV BIOL GENET, DEP BIOL, INDIANA UNIV, BLOOMINGTON, INDIANA 47405, USA**USA
JOURNAL: Genes and Development 3 (3): p399-414 1989
ISSN: 0890-9369
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The labial (la) gene of Drosophila melanogaster is necessary for the proper development of the embryonic (larval) and adult head. We have identified the lab transcription unit within the proximal portion of the %%%Antennapedia%%% Complex (ANT-C) by mapping the molecular lesions associated with chromosomally rearranged lab alleles. We present in molecular structure, nucleotide sequence, and temporal pattern of expression. In addition, using antibodies generated against a %%%fusion%%% protein, we show that in the embryo the lab protein is distributed in neural and epidermal cells of the procephalic lobe; in a discrete loop of the midgut; and in specific progenitor sensory cells of the clypeolabrum, thoracic segments, and tail region. The regions of lab expression in the developing cephalon represent nonsegmented domains that are anterior to and largely nonoverlapping with the domains of expression of the Deformed (Dfd) and proboscipedia (pb) genes, two other homeotic loci of the ANT-C that also function to direct the development of head structures. Furthermore, lab head expression is associated with the complex cellular movement of head involution, a process that not only is defective in lab- embryos, but the failure of which appears to be largely responsible for the defects observed in mutant embryos. Finally, we suggest that lab head expression provdies a molecular marker for an intercalary segment, an ancestral segment that has become morphologically indistinct during the evolution of the insect head.

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DIALOG(R)File 5:Biosis Previews(R)

09601019 BIOSIS NO.: 198987048910
COMBINATORIAL EXPRESSION OF A FTZ-ZEN %%%FUSION%%% PROMOTER SUGGESTS THE OCCURRENCE OF CIS INTERACTIONS BETWEEN GENES OF THE ANT-C
AUTHOR: RUSHLOW C (Reprint); LEVINE M
AUTHOR ADDRESS: DEP BIOL SCI, FAIRCHILD CENT, COLUMBIA UNIV, NEW YORK, NY 10027, USA**USA
JOURNAL: EMBO (European Molecular Biology Organization) Journal 7 (11): p

3479-3486 1988
ISSN: 0261-4189
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The nine homeobox genes contained within the %%%Antennapedia%%% gene complex (ANT-C) are precisely regulated during embryonic development. It is not known to what extent the physical linkage of these genes contributes to their normal patterns of expression. Here we show that cis regulatory elements associated with one homeobox gene can act over a long distance (.apprx. 20 kb) to influence the expression of another homeobox gene. Specifically, fushi tarazu (ftz) promoter elements can direct the periodic expression of the z2 gene, which normally shows a simple 'dorsal on/ventral off" pattern of expression. An 80 kb deletion within the ANT-C [Df(3R)LIN] juxtaposes the z2 and ftz promoters, resulting in a hybrid expression pattern whereby z2 transcripts are distributed within periodic stripes that are confined to dorsal and lateral tissues and not observed in the ventral mesoderm. This observation suggests that separate promoter elements of different genes can function in a combinatorial manner, and that the patterns of ANT-C gene expression might depend on cis regulatory interactions.

09556659 BIOSIS NO.: 198987004550
REGULATION AND FUNCTION OF THE DROSOPHILA SEGMENTATION GENE FUSHI TARAZU
AUTHOR: HIROMI Y (Reprint); GEHRING W J
AUTHOR ADDRESS: DEP BIOLOGICAL SCI, STANFORD UNIV, STANFORD, CALIF 94305, USA**USA
JOURNAL: Cell 50 (6): p963-974 1987
ISSN: 0092-8674
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The Drosophila segmentation gene fushi tarazu (ftz) is expressed in a pattern of seven stripes at the blastoderm stage. Two cis-acting control elements are required for this expression: the zebra element, which confers the striped pattern by mediating the effects of a subset of segmentation genes; and the upstream element, an enhancer element requiring ftz+ activity for its action. %%%Fusion%%% of the upstream element to a basal promoter results in activation of the heterologous promoter in a ftz-dependent striped pattern, supporting the idea that ftz regulates itself by acting through its enhancer. The upstream element can also confer expression patterns similar to that of the homeotic gene %%%Antennapedia%%%, suggesting that a similar element may play a role in the activation of %%%Antennapedia%%%.

08617896 BIOSIS NO.: 198783096787
MOLECULAR ANALYSIS OF THE DOMINANT HOMEOTIC %%%ANTENNAPEDIA%%% PHENOTYPE
AUTHOR: SCHNEUWLY S (Reprint); KUROIWA A; GEHRING W J
AUTHOR ADDRESS: DEP BIOLOGICAL SCI, PURDUE UNIV, WEST LAFAYETTE, INDIANA 47907, USA**USA
JOURNAL: EMBO (European Molecular Biology Organization) Journal 6 (1): p 201-206 1987
ISSN: 0261-4189
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Most of the dominant alleles of the homeotic gene %%%Antennapedia%%% (Antp) which show a transformation of antennae into legs are associated with large chromosomal inversions. To determine the molecular mechanisms underlying the dominant phenotype, one of the strongest Antp alleles (Antp73b) was studied in more detail. The mutant chromosome has been cloned and the structure of the inversion has been identified. The inversion breaks two genes apart: the Antp gene and a previously unidentified gene, tentatively called responsible for dominant phenotype (rfd), located at 84D1-2. The two genes are transcribed in opposite directions and the breakpoints lie within introns of both genes. Through the inversion event, a reciprocal exchange of the first exons including promoters occurred leading to the production of new transcripts. The transcripts containing the entire Antp protein coding region which have been fused to the promoter of the rfd gene are lost in revertants of the dominant phenotype indicating a correlation between this %%%fusion%%% gene and the dominant phenotype. The molecular structure of inversion Atnp73b suggests that the dominant phenotype arises via ectopic expression of the normal Antp protein due to a gene %%%fusion%%% event.

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08576164 BIOSIS NO.: 198783055055
LOCALIZATION OF THE %%%ANTENNAPEDIA%%% PROTEIN IN DROSOPHILA EMBRYOS AND IMAGINAL DISCS
AUTHOR: WIRZ J (Reprint); FESSLER L I; GEHRING W J
AUTHOR ADDRESS: BIOZENTRUM, UNIV BASEL, KLINGELBERGSTRASSE 70, CH-4056 BASEL, SWITZERLAND**SWITZERLAND
JOURNAL: EMBO (European Molecular Biology Organization) Journal 5 (12): p 3327-3334 1986
ISSN: 0261-4189
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Antibodies have been raised against a %%%fusion%%% protein containing the 3' region of the coding sequence of the %%%Antennapedia%%% (Antp) gene fused to .beta.-galactosidase. The distribution of the protein on whole mount embryos and imaginal discs of third instar larvae was examined by immunofluorescence. In young embryos, expression of the Antp protein was limited to the thoracic segements in the epidermis, whereas it was found in all neuromeres of head, thorax and abdomen. At

the end of embryogenesis, the Antp protein mainly accumulated in the ventral nervous system in certain parts of the thoracic neuromeres, from posterior T1 to anterior T3, with a gap in posterior T2. Comparison of Antp protein distribution in nervous systems from wild-type and Df P9 embryos, lacking the genes of the Bithorax-complex (BX-C), revealed a pattern of expression which indicated that the BX-C represses Antp in the posterior segments with the exception of the last abdominal neuromeres (A8-9) which are regulated independently. The protein pattern in nervous systems from Sex combs reduced (ScrxF9) mutant embryos was indistinguishable from that found in wild-type embryos; thus, neurogenic expression of Antp in T1 and the more anterior segments does not appear to be under the control of Scr+. All imaginal discs derived from the three thoracic segments express Antp protein. The distribution was distinct in each disc; strongest expression was observed in the proximal parts of the discs. In the leg discs the protein distribution seemed to be compartmentally restricted, whereas in the wing disc this was not the case. Antp protein was not detected in the eye-antennal disc. In embryos, as well as in imaginal discs, the protein is localized in the nucleus.

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DIALOG(R)File 5:Biosis Previews(R)

08575084 BIOSIS NO.: 198783053975
AN INVERSION THAT DISRUPTS THE %%%ANTENNAPEDIA%%% GENE CAUSES ABNORMAL STRUCTURE AND LOCALIZATION OF RNA
AUTHOR: FRISCHER L E (Reprint); HAGEN F S; GARBER R L
AUTHOR ADDRESS: DEP GENET, UNIV WASH, SEATTLE, WASH 98195, USA**USA
JOURNAL: Cell 47 (6): p1017-1024 1986
ISSN: 0092-8674
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Mutations in Drosphila homeotic genes lead to the developmental replacement of one normal body part by another. We have examined the mechanism by which a dominant allele of the %%%Antennapedia%%% (Antp) gene causes the antennae to be replaced by legs. Normal Antp gene activity is required for thoracic but not for head development. We demonstrate that the Antp73b inversion mutation results in Antp transcription in the head. Antp transcripts found in this abnormal location are of two types: normal-sized Antp RNAs and %%%fusion%%% RNAs joining Antp exons (including the protein-coding region) to 5' exons from another gene. This foreign gene is normally expressed in the head, suggesting the cause for abnormal activation of Antp. The result is a change of cell identity from head to thorax.

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DIALOG(R)File 5:Biosis Previews(R)

07347996 BIOSIS NO.: 198478083403
CLONING AND TRANSCRIPTIONAL ANALYSIS OF THE SEGMENTATION GENE FUSHI TARAZU OF DROSOPHILA
AUTHOR: KUROIWA A (Reprint); HAFEN E; GEHRING W J

AUTHOR ADDRESS: DEP CELL BIOL, BIOZENTRUM, UNIV BASEL, KLINGELBERGSTRASSE 70, CH-4056 BASEL, SWITZERLAND**SWITZERLAND
JOURNAL: Cell 37 (3): p825-832 1984
ISSN: 0092-8674
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: A study of the %%%Antennapedia%%% (Antp) locus found that one of the 3' Antp exons has weak cross-homology to another gene affecting segmentation, fushi tarazu (ftz; meaning not enough segments), which is 30 kb [kilobase] to the left of Antp. Homozygous ftz- embryos die before hatching and lack alternate body segments. The reduced number of segments results from the %%%fusion%%% of the anterior portion of 1 segment with the posterior portion of the next segment. The ftz gene encodes a single 1.9 kb poly(A)+ RNA expressed exclusively from the early blastoderm to gastrula stages of embryonic development. The structure of the ftz gene was analyzed by S1 nuclease mapping and by restriction mapping of a c[complementary]DNA clone. The ftz gene consists of 2 exons, and it is the 3' exon that cross-hybridizes with the 3' exon of Antp. The role of ftz in cell determination is discussed.
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1/7/1
DIALOG(R)File 5:Biosis Previews(R)

0021246546 BIOSIS NO.: 200900587983
The Internalization of %%%Antennapedia%%%-Green Fluorescence %%%Fusion%%% Protein into Human Umbilical Vein Epithelial Cells
AUTHOR: Hartman P A (Reprint); Porta M J; Fenner B M; Shurina R D
AUTHOR ADDRESS: Wheeling Jesuit Univ, Wheeling, WV USA**USA
JOURNAL: Molecular Biology of the Cell 17 (Suppl. S): 2006 2006
CONFERENCE/MEETING: 46th Annual Meeting of the American-Society-for-Cell-Biology San Diego, CA, USA December 09 -13, 2006; 20061209
SPONSOR: Amer Soc Cell Biol
ISSN: 1059-1524
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

1/7/2
DIALOG(R)File 5:Biosis Previews(R)

0021210653 BIOSIS NO.: 200900552090
CONFORMATION OF FUSOGENIC PEPTIDES AND AN ANTISENSE OLIGONUCLEOTIDE IN COMPLEX IN THE PRESENCE OF MICELLES
AUTHOR: Laczko-Hollosi I (Reprint); Toth G K; Ilyes E; Hollosi M
AUTHOR ADDRESS: Univ Szeged, Inst Biophys, Biol Res Ctr, Szeged, Hungary** Hungary
JOURNAL: Journal of Peptide Science 10 (Suppl. S): p196 2004 2004
CONFERENCE/MEETING: 3rd International Peptide Symposium/28th European Peptide Symposium Prague, CZECH REPUBLIC September 05 -10, 2004; 20040905
ISSN: 1075-2617

DOCUMENT TYPE: Meeting; Meeting Poster
RECORD TYPE: Citation
LANGUAGE: English

1/7/3
DIALOG(R)File 5:Biosis Previews(R)

0021153002 BIOSIS NO.: 200900494439
Novel nanoparticle %%%fusion%%% protein achieves normal p21 delivery to p53/p21 mutated tumors resulting in their eradication.
AUTHOR: Kousparou Christina (Reprint); Stylianou Spyros; Deonarain Mahendra ; Epenetos Agamemnon
AUTHOR ADDRESS: Bank Cyprus Oncol Ctr, Nicosia, Cyprus**Cyprus
JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 50 p415-416 APR 2009 2009
CONFERENCE/MEETING: 100th Annual Meeting of the American-Association-for-Cancer-Research Denver, CA, USA April 18 -22, 2009; 20090418
SPONSOR: Amer Assoc Canc Res
ISSN: 0197-016X
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

1/7/4
DIALOG(R)File 5:Biosis Previews(R)

0021137457 BIOSIS NO.: 200900478894
Caveolin peptides and their use as therapeutics
AUTHOR: Sessa William C; Anonymous
AUTHOR ADDRESS: Madison, CT USA**USA
JOURNAL: Official Gazette of the United States Patent and Trademark Office Patents FEB 17 2009 2009
PATENT NUMBER: US 07494976 PATENT DATE GRANTED: February 24, 2009 20090224
PATENT CLASSIFICATION: 514-12 PATENT ASSIGNEE: Yale University
PATENT COUNTRY: USA
ISSN: 0098-1133
DOCUMENT TYPE: Patent
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The present invention relates generally to compositions and methods useful for treating various conditions and afflictions, such as inflammation and cancer. More specifically, the present invention relates to compositions and methods of treatment which utilize peptides comprising at least one caveolin scaffolding domain. Even more specifically, the present invention relates to compositions of %%%fusion%%% peptides comprising the %%%antennapedia%%% homeodomain fused to a caveolin scaffolding domain and to methods of using these peptides to treat various conditions and afflictions.

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DIALOG(R)File 5:Biosis Previews(R)

0019797722 BIOSIS NO.: 200700457463
Modulation of pulmonary vascular smooth muscle cell phenotype in hypoxia: role of cGMP-dependent protein kinase
AUTHOR: Zhou Weilin (Reprint); Dasgupta Chiranjib; Negash Sewite; Raj J Usha
AUTHOR ADDRESS: Harbor UCLA Med Ctr, Los Angeles Biomed Res Inst, Div Neonatol, 1124 W Carson St, Torrance, CA 90502 USA**USA
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JOURNAL: American Journal of Physiology - Lung Cellular and Molecular Physiology 292 (6): pL1459-L1466 JUN 2007 2007
ITEM IDENTIFIER: doi:10.1152/ajplung.00143.2006
ISSN: 1040-0605
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Chronic hypoxia triggers pulmonary vascular remodeling, which is associated with a modulation of the vascular smooth muscle cell (SMC) phenotype from a contractile, differentiated to a synthetic, dedifferentiated state. We previously reported that acute hypoxia represses cGMP- dependent protein kinase (PKG) expression in ovine fetal pulmonary venous SMCs (FPVSMCs). Therefore, we tested if altered expression of PKG could explain SMC phenotype modulation after exposure to hypoxia. Hypoxia- induced reduction in PKG protein expression strongly correlated with the repressed expression of SMC phenotype markers, myosin heavy chain (MHC), calponin, vimentin, alpha-smooth muscle actin (alpha SMA), and thrombospondin (TSP), indicating that hypoxic exposure of SMC induced phenotype modulation to dedifferentiated state, and PKG may be involved in SMC phenotype modulation. PKG- specific small interfering RNA (siRNA) transfection in FPVSMCs significantly attenuated calponin, vimentin, and MHC expression, with no effect on alpha SMA and TSP. Treatment with 30 mu M Drosophila %%%Antennapedia%%% (DT- 3), a membrane- permeable peptide inhibitor of PKG, attenuated the expression of TSP, MHC, alpha SMA, vimentin, and calponin. The results from PKG siRNA and DT-3 studies indicate that hypoxia- induced reduction in protein expression was also similarly impacted by PKG inhibition. Overexpression of PKG in FPVSMCs by transfection with a full- length PKG construct tagged with green fluorescent %%%fusion%%% protein (PKG- GFP) reversed the effect of hypoxia on the expression of SMC phenotype marker proteins. These results suggest that PKG could be one of the determinants for the expression of SMC phenotype marker proteins and may be involved in the maintenance of the differentiated phenotype in pulmonary vascular SMCs in hypoxia.

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DIALOG(R)File 5:Biosis Previews(R)

0019636427 BIOSIS NO.: 200700296168
Driving forces in the delivery of penetratin conjugated G protein fragment
AUTHOR: Albrizio Stefania; Giusti Laura; D'Errico Gerardino; Esposito Cinzia; Porchia Francesca; Caliendo Gabriella; Novellino Ettore; Mazzoni Maria R; Rovero Paolo; D'Ursi Anna M (Reprint)

AUTHOR ADDRESS: Univ Salerno, Dept Pharmaceut Sci, I-84084 Fisciano, Italy
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JOURNAL: Journal of Medicinal Chemistry 50 (7): p1458-1464 APR 5 2007 2007
ISSN: 0022-2623
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A42 is a %%%chimera%%% peptide consisting of G alpha(s)(374-394)C(379)Athe 21-mer C terminus of the G alpha(s) protein, able of adenosine inhibitory activityand penetratinthe 16 residue fragment, derived from the homeodomain of the Drosophila transcription factor %%%Antennapedia%%%. A42 is able to cross cell membranes and to inhibit A(2A) and A(2B) adenosine and beta-adrenergic receptor stimulated camps (D'Ursi et al. Mol. Pharmacol. 2006, 69, 727-36). Here we present an extensive biophysical study of A42 in different membrane mimetics, with the objective to evaluate the molecular mechanisms which promote the membrane permeation. Fluorescence, CD, and NMR data were acquired in the presence of negatively charged and zwitterionic sodium dodecyl sulfate and dodecylphosphocholine surfactants. To validate the spectroscopic results in a larger scale, fluorescence microscopy experiments were performed on negatively charged and zwitterionic dipalmitoylphosphatidylglycerol and dipalmitoylphosphatidylcholine vesicles. Our results show that the internalization of A42 is mainly driven by electrostatic interactions, hydrophobic interactions playing only a secondary, sinergistic role. The distribution of the charges along the molecule has an important role, highlighting that internalization is a process which requires a specific matching of peptide and membrane properties.

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0019499382 BIOSIS NO.: 200700159123
Elaboration of new SELEX modification and its usage for selection of DNA sequences recognized by %%%Antennapedia%%% homeodomain
AUTHOR: Ershova A S (Reprint); Lavrova N; Tikhonova T; Kuznetsova A Yu; Mostovenko E; Alexeevsky A; Lunin V G; Karyagina A S
AUTHOR ADDRESS: Moscow MV Lomonosov State Univ, Belozersky Inst Physicochem Biol, Moscow, Russia**Russia
JOURNAL: Doklady Rossiiskoi Akademii Sel'skokhozyaistvennykh Nauk (5): p5-9 SEP-OCT 2006 2006
ISSN: 0869-6128
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: Russian

ABSTRACT: An original modification of SELEX procedure is suggested The procedure is applicable to a %%%fusion%%% protein consisting of two domains, the cellulose binding domainfrom Anaerocellum thermophilum and a DNA-binding domain. This protein was immobilized by non-covalent interactions between cellulose carrier and cellulose binding domain. The developed SELEX procedure was used for selection of DNA fragments bound by %%%Antennapedia%%% homeodomain. The consensus sequence of selected

fragments is 5-GGANAANNNA-3'.

1/7/8
DIALOG(R)File 5:Biosis Previews(R)

18901117 BIOSIS NO.: 200600246512
In vivo delivery of a XIAP (BIR3-RING) %%%fusion%%% protein containing the protein transduction domain protects against neuronal death induced by seizures
AUTHOR: Li Tianfu; Fan Yongfeng; Luo Yumin; Xiao Baoguo; Lu Chuanzhen (Reprint)
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JOURNAL: Experimental Neurology 197 (2): p301-308 FEB 2006 2006
ISSN: 0014-4886
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The prevention of cell apoptosis is a promising strategy for neuroprotection against brain injury in seizures. X-linked inhibitor of apoptosis protein (XIAP) is regarded as the most potent inhibitor of cell apoptosis. In the present study, we fused the protein transduction domain (PTD) of %%%Antennapedia%%% Homeodomain of Drosophila (AntpHD) to XIAP (BIR3-RING) and explored the neuroprotective effect of XIAP in rats with seizures induced by kainic acid (KA). KA triggered neuronal death in the ipsilateral CA3 subfield of the hippocampus and activation of caspase-3 and -9. PTD-XIAP %%%fusion%%% protein can be delivered into cos7 cells in vitro. We used intraperitoneal injection to deliver the PTD-XIAP %%%fusion%%% protein which can enter into brain, significantly decrease the TLYNEL positive cells and increase the number Of Surviving cells in the ipsilateral CA3 subfield of the hippocampus at 24 In after KA-induced seizures. Furthermore, PTD-XIAP %%%fusion%%% protein attenuated activated caspase-3 and -9. These results demonstrate the neuroprotective effect of PTD-XIAP %%%fusion%%% protein against brain injury possibly through the inhibition of caspase. The significance of these findings in the treatment of epilepsy still needs to be extensively studied. (c) 2005 Elsevier Inc. All rights reserved.

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DIALOG(R)File 5:Biosis Previews(R)

18660452 BIOSIS NO.: 200600005847
Glycogen synthase kinase 3 beta inhibits myocardin dependent transcription and hypertrophy induction through site-specific phosphorylation
AUTHOR: Badorff Cornel; Seeger Florian H; Zeiher Andreas M; Dimmeler Stefanie (Reprint)
AUTHOR ADDRESS: Univ Frankfurt, Dept Mol Cardiol, Theodor Stern Kai 7, D-60590 Frankfurt, Germany**Germany
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JOURNAL: Circulation Research 97 (7): p645-654 SEP 30 2005 2005
ISSN: 0009-7330

DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Cardiomyocyte hypertrophy is transcriptionally controlled and inhibited by glycogen synthase kinase 3 beta (GSK3 beta). Myocardin is a muscle-specific transcription factor with yet unknown relation to hypertrophy. Therefore, we investigated whether myocardin is sufficient to induce cardiomyocyte hypertrophy and whether myocardin is regulated by GSK3 beta through site-specific phosphorylation. Adenoviral myocardin overexpression induced cardiomyocyte hypertrophy in neonatal rat cardiomyocytes, with increased cell size, total protein amount, and transcription of atrial natriuretic factor (ANF). In vitro and in vivo (HEK 293 cells) kinase assays with synthetic peptides and full-length myocardin demonstrated that myocardin was a "primed" GSK3 beta substrate, with serines 455 to 467 and 624 to 636 being the major GSK3 beta phosphorylation sites. Myocardin-induced ANF transcription and increase in total protein amount were enhanced by GSK3 beta blockade (10 mmol/L LiCl), indicating that GSK3 beta inhibits myocardin. A GSK3 beta phosphorylation-resistant myocardin mutant (8xA) activated ANF transcription twice as potently as wildtype myocardin under basal conditions with GSK3 beta being active. Conversely, a GSK3 beta phospho-mimetic myocardin mutant (8xD) was transcriptionally repressed after GSK3 beta blockade, indicating that GSK3 beta phosphorylation at the sites identified inhibits myocardin transcriptional activity. GAL4-myocardin %%%fusion%%% constructs demonstrated that GSK3 beta phosphorylation reduced the intrinsic myocardin transcriptional activity. A cell-permeable (%%%Antennapedia%%% protein transduction tag) peptide containing the mapped myocardin GSK3 beta motifs 624 to 636 induced hypertrophy of cultured cardiomyocytes, suggesting that the peptide acted as substrate-based GSK3 beta inhibitor in cardiomyocytes. Therefore, we conclude that the GSK3 beta-myocardin interaction constitutes a novel molecular control of cardiomyocyte hypertrophy. Phosphorylation by GSK3 beta comprises a novel post-transcriptional regulatory mechanism of myocardin.

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DIALOG(R)File 5:Biosis Previews(R)

18570799 BIOSIS NO.: 200510265299
Inhibition of a cathepsin L-like cysteine protease by a %%%chimeric%%% propeptide-derived inhibitor
AUTHOR: Godat Emmanuel; Chowdhury Shafinaz; Lecaille Fabien; Belghazi Maya; Purisima Enrico O; Lalmanach Gilles (Reprint)
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JOURNAL: Biochemistry 44 (31): p10486-10493 AUG 9 2005 2005
ISSN: 0006-2960
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Like other papain-related cathepsins, congopain from Trypanosoma congolense is synthesized as a zymogen. We have previously identified a

proregion-derived peptide (Pcp27), acting as a weak and reversible inhibitor of congopain. Pcp27 contains a 5-mer YHNGA motif, which is essential for selectivity in the inhibition of its mature form [Lalmanach, G., Lecaille, F., Chagas, J. R., Authie, E., Scharfstein, J., Juliano, M. A., and Gauthier, F. (1998) J. Biol. Chem. 273, 25112-25116]. In the work presented here, a homology model of procongopain was generated and subsequently used to model a %%%chimeric%%% 50-mer peptide (called H3-Pcp27) corresponding to the covalent linkage of an unrelated peptide (H3 helix from %%%Antennapedia%%%) to Pcp27. Molecular simulations suggested that H3-Pcp27 (pI = 9.99) maintains an N-terminal helical conformation, and establishes more complementary electrostatic interactions (E-coul = -25.77 kcal/mol) than 16N-Pcp27, the 34-mer Pcp27 sequence plus the 16 native residues upstream from the proregion (E-coul = 0.20 kcal/mol), with the acid catalytic domain (pI = 5.2) of the mature enzyme. In silico results correlated with the significant improvement of congopain inhibition by H3-Pcp27 (K; = 24 nM), compared to 16N-Pep27 (K-i = 1 mu M). In addition, virtual alanine scanning of H3 and 16N identified the residues contributing most to binding affinity. Both peptides did not inhibit human cathepsins B and L. In conclusion, these data support the notion that the positively charged H3 helix favors binding, without modifying the selectivity of Pcp27 for congopain.

17803591 BIOSIS NO.: 200400174348
Internalization of caveolin-1 scaffolding domain facilitated by %%%Antennapedia%%% homeodomain attenuates PAF-induced increase in microvessel permeability.
AUTHOR: Zhu Longkun; Schwegler-Berry Diane; Castranova Vince; He Pingnian (Reprint)
AUTHOR ADDRESS: Dept. of Physiology and Pharmacology, School of Medicine, West Virginia Univ., Health Sciences Center North, Morgantown, WV, 26506-9229, USA**USA
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JOURNAL: American Journal of Physiology 286 (1 Part 2): pH195-H201 January 2004 2004
MEDIUM: print
ISSN: 0002-9513 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We demonstrated previously that inhibition of endothelial nitric oxide synthase (NOS), using pharmacological inhibitors, attenuated the ionomycin- and ATP-induced increases in microvessel permeability (Am J Physiol Heart Circ Physiol 272: H176-H185, 1997). Recently, the scaffolding domain of caveolin-1 (CAV) has been implicated as a negative regulator of endothelial NOS (eNOS). To examine the role of CAV-eNOS interaction in regulation of permeability in intact microvessels, the effect of internalized CAV on the platelet-activating factor (PAF)-induced permeability increase was investigated in rat mesenteric venular microvessels. Internalization of CAV was achieved by perfusion of individual vessels using a %%%fusion%%% peptide of CAV with %%%Antennapedia%%% homeodomain (AP-CAV) and visualized by fluorescence

imaging and electron microscopy. Changes in microvessel permeability were evaluated by measuring hydraulic conductivity (LP) in individually perfused microvessels. We found that the PAF (10 nM)-induced LP increase was significantly attenuated from 6.0+-0.9 (n=7) to 2.0+-0.3 (n=5) times control after microvessels were perfused with 10 muM AP-CAV for 2 h. The magnitude of this reduction is comparable with that of the inhibitory effect of Nomega-monomethyl-L-arginine on the PAF-induced LP increase. In contrast, perfusion with 10 muM AP alone for 2 h modified neither basal LP nor the vessel response to PAF. These results indicate that CAV plays an important role in regulation of microvessel permeability. The inhibitory action of CAV on permeability increase might be attributed to its direct inactivation of eNOS. In addition, this study established a method for studying protein-protein interaction-induced functional changes in intact microvessels and demonstrated AP as an efficient vector for translocation of peptide across the cell membrane in vivo.

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DIALOG(R)File 5:Biosis Previews(R)

17714325 BIOSIS NO.: 200400095082
Signaling and protein associations of a cell permeable CD40 complex in B cells.
AUTHOR: Zoog Stephen J; Papov Vladimir V; Pullen Steven S; Jakes Scott; Kehry Marilyn R (Reprint)
AUTHOR ADDRESS: IDEC Pharmaceuticals Corp., 3010 Science Park Road, San Diego, CA, 92121, USA**USA
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JOURNAL: Molecular Immunology 40 (10): p681-694 January 2004 2004
MEDIUM: print
ISSN: 0161-5890 _(ISSN print)
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Signaling through the CD40 receptor activates diverse molecular pathways in a variety of immune cell types. To study CD40 signaling complexes in B cells, we produced soluble CD40 cytoplasmic domain multimers that translocate across cell membranes and engage intra-cellular CD40 signaling pathways. As visualized by fluorescence microscopy, rapid transduction of recombinant %%%Antennapedia%%% -isoleucine zipper (Izip)-CD40 cytoplasmic domain %%%fusion%%% protein (Antp-CD40) occurred in both the DND39 B cell line and human tonsillar B cells. Upon cellular entry, Antp-CD40 activated NF-kappaB-dependent transcription, induced proteolytic processing of p100 to the p52/NF-kappaB2 subunit, and increased expression of CD80 and CD54 on the surface of B cells. Antp-CD40 transduction of B cells did not, however, activate detectable levels of p38 mitogen-activated protein kinase or c-Jun N-terminal kinase and did not up-regulate CD95 expression. Analysis of Antp-CD40 complexes recovered from transduced B cells revealed that Antp-CD40 associated with endogenous TRAF3 and Ku proteins. Multimerization of Antp-CD40, or extensive clustering of transmembrane CD40, diminished the disruptive effect of the T254A mutation in the TRAF2/3 binding site of the CD40 cytoplasmic domain. Taken together, these results indicate that Antp-CD40 mimics some of the natural CD40 signaling pathways in B cells by assembling partially functional

signaling intermediates that do not require plasma membrane localization. We present a novel approach for delivering pre-activated, soluble receptor cytoplasmic domains into cells and recovering intact signaling complexes for molecular analysis.

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DIALOG(R)File 5:Biosis Previews(R)

17472747 BIOSIS NO.: 200300427591
Enhancing the efficacy of chemotherapeutic drugs by the suppression of antiapoptotic cellular defense.
AUTHOR: Minko T (Reprint); Dharap S S; Fabbricatore A T
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JOURNAL: Cancer Detection and Prevention 27 (3): p193-202 2003 2003
MEDIUM: print
ISSN: 0361-090X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The study was aimed at evaluating the combination of a traditional anticancer drug doxorubicin (DOX) with a suppressor of antiapoptotic cellular defense-synthetic peptide corresponding to the minimal sequence of BCL-2 homology 3 (BH3) domain. BH3 peptide was delivered into cells by %%%fusion%%% with a peptide corresponding to the %%%Antennapedia%%% (Ant) internalization sequence. The cytotoxicity of DOX, Ant-BH3 and Ant-BH3 mixed in with DOX, mitochondrial transmembrane potential, expression of genes encoding pro- and antiapoptotic members of BCL-2 protein family and caspases, caspases activity, apoptosis induction were assessed in human ovarian carcinoma cells. It was found that the combination in one drug formulation of DOX and Ant-BH3 produced two main effects: (1) enhancing the apoptosis induction by an anticancer drug, and (2) preventing the development of antiapoptotic cellular drug resistance. The results confirmed that anticancer drug-BH3 combination might form the basis for a new advanced anticancer proapoptotic drug delivery systems.

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DIALOG(R)File 5:Biosis Previews(R)

17300296 BIOSIS NO.: 200300258940
In vivo delivery of caveolin-1 scaffolding domain attenuates PAF-induced increase In microvessel permeability.
AUTHOR: Zhu Longkun (Reprint); He Pingnian
AUTHOR ADDRESS: Physiology and Pharmacology, West Virginia University, Health Sciences Center, Morgantown, WV, 26506-9229, USA**USA
AUTHOR E-MAIL ADDRESS: phe@hsc.wvu.edu; phe@hsc.wvu.edu
JOURNAL: FASEB Journal 17 (4-5): pAbstract No. 101.7 March 2003 2003
MEDIUM: e-file
CONFERENCE/MEETING: FASEB Meeting on Experimental Biology: Translating the Genome San Diego, CA, USA April 11-15, 2003; 20030411

SPONSOR: FASEB
ISSN: 0892-6638 _(ISSN print)
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We demonstrated previously that the inhibition of nitric oxide synthase (NOS) using pharmacological inhibitor attenuated the ionomycin-and ATP-induced increases in microvessel permeability. Recently the scarffolding domain of caveolin-1 (CAV) has been implicated as a negative regulator of eNOS in endothelial cells. To examine the role of CAV-NOS interaction in the regulation of permeability in intact microvessels, the effect of internalized CAV on PAF-induced permeability increase was investigated in rat mesenteric venular microvessels. The in vivo delivery of CAV was achieved by perfusing individual vessels with a %%%fusion%%% peptide of CAV with %%%antennapedia%%% homeodomain (AP). Changes in microvessel permeability were evaluated by measuring hydraulic conductivity (Lp). Results demonstrated that 2h perfusion of AP-CAV (10 muM) significantly attenuated the PAF (10 nM)-induced Lp increase from 6.0 +- 0.9 (n=7) to 2.0 +- 0.3 (n=5) times the control value. The magnitude of this reduction is comparable with that of the inhibitory effect of L-NMMA on PAF-induced Lp increase. In contrast, perfusion of AP (10 muM) alone for 2h modified neither basal Lp nor the vessel response to PAF. These results indicated that CAV plays an important role in the regulation of microvessel permeability. Its inhibitory action on the permeability increase might be attributed to the inhibition of endothelial NOS activity.

17136637 BIOSIS NO.: 200300095356
Escherichia coli K1 internalization via caveolae requires caveolin-1 and protein kinase Calpha interaction in human brain microvascular endothelial cells.
AUTHOR: Sukumaran Sunil K; Quon Michael J; Prasadarao Nemani V (Reprint)
AUTHOR ADDRESS: Div. of Infectious Diseases, Children's Hospital, 4650 Sunset Blvd., MS 51, Los Angeles, CA, 90027, USA**USA
AUTHOR E-MAIL ADDRESS: pnemani@chla.usc.edu
JOURNAL: Journal of Biological Chemistry 277 (52): p50716-50724 December 27, 2002 2002
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The morbidity and mortality associated with Escherichia coli K1 meningitis during the neonatal period have remained significant over the last decade and are once again on the rise. Transcytosis of brain microvascular endothelial cells (BMEC) by E. coli within an endosome to avoid lysosomal %%%fusion%%% is crucial for dissemination into the central nervous system. Central to E. coli internalization of BMEC is the expression of OmpA (outer membrane protein A), which interacts with its receptor for the actin reorganization that leads to invasion. However,

nothing is known about the nature of the signaling events for the formation of endosomes containing E. coli K1. We show here that E. coli K1 infection of human BMEC (HBMEC) results in activation of caveolin-1 for bacterial uptake via caveolae. The interaction of caveolin-1 with phosphorylated protein kinase Calpha (PKCalpha) at the E. coli attachment site is critical for the invasion of HBMEC. Optical sectioning of confocal images of infected HBMEC indicates continuing association of caveolin-1 with E. coli during transcytosis. Overexpression of a dominant-negative form of caveolin-1 containing mutations in the scaffolding domain blocked the interaction of phospho-PKCalpha with caveolin-1 and the E. coli invasion of HBMEC, but not actin cytoskeleton rearrangement or the phosphorylation of PKCalpha. The interaction of caveolin-1 with phospho-PKCalpha was completely abrogated in HBMEC overexpressing dominant-negative forms of either focal adhesion kinase or PKCalpha. Treatment of HBMEC with a cell-permeable peptide that represents the scaffolding domain, which was coupled to an %%%antennapedia%%% motif of a Drosophila transcription factor significantly blocked the interaction of caveolin-1 with phospho-PKCalpha and E. coli invasion. These results show that E. coli K1 internalizes HBMEC via caveolae and that the scaffolding domain of caveolin-1 plays a significant role in the formation of endosomes.

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DIALOG(R)File 5:Biosis Previews(R)

16983178 BIOSIS NO.: 200200576689
HIV-1 Vpr displays natural protein-transducing properties: Implications for viral pathogenesis
AUTHOR: Sherman Michael P; Schubert Ulrich; Williams Samuel A; de Noronha Carlos M C; Kreisberg Jason F; Henklein Peter; Greene Warner C (Reprint)
AUTHOR ADDRESS: Gladstone Institute of Virology and Immunology, P.O. Box 419100, San Francisco, CA, 94141-9100, USA**USA
JOURNAL: Virology 302 (1): p95-105 October 10, 2002 2002
MEDIUM: print
ISSN: 0042-6822
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The 14-kDa Vpr protein of human immunodeficiency virus type 1 (HIV-1) serves multiple functions in the retroviral life cycle, including the enhancement of viral replication in nondividing macrophages, the induction of G2 cell-cycle arrest in proliferating T lymphocytes, and the modulation of HIV-1-induced apoptosis. Extracellular Vpr has been detected in the sera and cerebral spinal fluid of HIV-infected patients. However, it is not known whether such forms of Vpr are biologically active. Vpr contains a carboxy-terminal basic amino acid rich segment stretch that is homologous to domains that mediate the energy-and receptor-independent cellular uptake of polypeptides by a process termed protein transduction. Similar functional protein-transducing domains are present in HIV-1 Tat, herpes simplex virus-1 DNA-binding protein VP22, and the Drosophila %%%antennapedia%%% homeotic transcription factor. We now demonstrate effective transduction of biologically active, synthetic Vpr (sVpr) as well as the Vpr-beta-galactosidase %%%fusion%%% protein. However, in contrast to other transducing proteins, Vpr transduction is

not enhanced by protein denaturation, and Vpr's carboxy-terminal basic domain alone is not sufficient for its transduction across biological membranes. In contrast, the full-length Vpr protein effectively transduces a broad array of cells, leading to dose-dependent G2 cell-cycle arrest and apoptosis. Addition of Vpr into the extracellular medium also rescues the replication of Vpr-deficient strains of HIV-1 in human macrophage cultures. Native Vpr may thus be optimized for protein transduction, a feature that might enhance and extend the pathological effects of HIV infection.

1/7/17
DIALOG(R)File 5:Biosis Previews(R)

16963879 BIOSIS NO.: 200200557390
Conformational studies of %%%chimeric%%% cell penetrating peptides in membrane mimicking environment
AUTHOR: Ruzza P (Reprint); Elardo S (Reprint); Calderan A (Reprint); Donella-Deana A; Crisma M (Reprint); Brunati A M; Massimino M L; Pinna L A; Borin G (Reprint)
AUTHOR ADDRESS: Biopolymer Research Centre, CNR, Department of Organic Chemistry, University of Padova, Padova, Italy**Italy
JOURNAL: Journal of Peptide Science 8 (Supplement): pS204 2002 2002
MEDIUM: print
CONFERENCE/MEETING: 27th European Peptide Symposium Sorrento, Italy August 31-September 06, 2002; 20020831
ISSN: 1075-2617
DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster
RECORD TYPE: Citation
LANGUAGE: English

1/7/18
DIALOG(R)File 5:Biosis Previews(R)

16526103 BIOSIS NO.: 200200119614
%%%Antennapedia%%%/HS1 %%%chimeric%%% phosphotyrosyl peptide: Conformational properties, binding capability to c-Fgr SH2 domain and cell permeability
AUTHOR: Ruzza Paolo (Reprint); Donella-Deana Arianna; Calderan Andrea; Brunati Annamaria; Massimino Maria Lina; Elardo Stefano; Mattiazzo Alessio; Pinna Lorenzo A; Borin Gianfranco
AUTHOR ADDRESS: Biopolymers Research Center, CNR, Via Marzolo 1, Padova, 35131, Italy**Italy
JOURNAL: Biopolymers 60 (4): p290-306 2001 2001
MEDIUM: print
ISSN: 0006-3525
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: With the aim of interfering with the signaling pathways mediated by the SH2 domains of Src-like tyrosine kinases, we synthesized a tyrosyl-phospho decapeptide, corresponding to the sequence 392-401 of HS1 protein, which inhibits the secondary phosphorylation of HS1 protein

catalyzed by the Src-like kinases c-Fgr or Lyn. This phospho-peptide was modified to enter cells by coupling to the third helix of %%%Antennapedia%%% homeodomain, which is able to translocate across cell membranes. Here we present CD and fluorescence studies on the conformational behavior in membrane-mimicking environments and on lipid interactions of %%%Antennapedia%%% fragment and its %%%chimeric%%% phosphorylated and unphosphorylated derivatives. These studies evidenced that electrostatic rather than amphiphilic interactions determine the peptide adsorption on lipids. Experiments performed with recombinant protein containing the SH2 domain of c-Fgr fused with GST and with isolated erythrocyte membranes demonstrated that the presence of the N-terminal %%%Antennapedia%%% fragment only slightly affects the binding of the phospho-HS1 peptide to the SH2 domain. In fact, it has been shown that in isolated erythrocyte membranes, both phospho-HS1 peptide and its %%%chimeric%%% derivative greatly affect either the SH2-mediated recruitment of the c-Fgr to the transmembrane protein band 3 and the following phosphorylation of the protein catalyzed by the Src-like kinase c-Fgr. The ability of the %%%chimeric%%% phospho-peptide to enter cells has been demonstrated by confocal microscopy analysis.

16236710 BIOSIS NO.: 200100408549
The BH3 domain of BAD fused to the %%%Antennapedia%%% peptide induces apoptosis via its alpha helical structure and independent of Bcl-2
AUTHOR: Schimmer A D; Hedley D W; Chow S; Pham N -A; Chakrabartty A; Bouchard D; Mak T W; Trus M R; Minden M D (Reprint)
AUTHOR ADDRESS: Princess Margaret Hospital, 610 University Ave., Room 9-111, Toronto, ON, M5G2M9, Canada**Canada
JOURNAL: Cell Death and Differentiation 8 (7): p725-733 July, 2001 2001
MEDIUM: print
ISSN: 1350-9047
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Since the over-expression of Bcl-2 is a common cause of multi-drug resistance, cytotoxic peptides that overcome the effects of Bcl-2 may be clinically useful. We harnessed the death-promoting alpha helical properties of the BH3 domain of BAD by fusing it to the %%%Antennapedia%%% (ANT) domain, which allows for cell entry (ANTBH3BAD). Treatment of 32D cells with the ANTBH3BAD peptide results in a 99% inhibition of colony formation. No significant toxicity is observed after treatment with ANT or BH3BAD alone. A mutant %%%fusion%%% peptide unable to bind Bcl-2 induces cell death as effectively as the wild-type ANTBH3BAD. Furthermore, 32D cells over-expressing Bcl-2 show no resistance to the ANTBH3BAD peptide. Therefore, the toxicity of the peptide was independent of the Bcl-2 pathway. We demonstrate that the toxicity of the peptide is due to its alpha helicity that disrupts mitochondrial function. Since this peptide overcomes major forms of drug resistance, it may be therapeutically useful if appropriately targeted to malignant cells.

1/7/20
DIALOG(R)File 5:Biosis Previews(R)

16117735 BIOSIS NO.: 200100289574
Interaction and structure induction of cell-penetrating peptides in the presence of phospholipid vesicles
AUTHOR: Magzoub Mazin; Kilk Kalle; Eriksson L E Goran; Langel Ulo; Graslund Astrid (Reprint)
AUTHOR ADDRESS: Department of Biochemistry and Biophysics, Arrhenius Laboratories, Stockholm University, S-106 91, Stockholm, Sweden**Sweden
JOURNAL: Biochimica et Biophysica Acta 1512 (1): p77-89 2 May, 2001 2001
MEDIUM: print
ISSN: 0006-3002
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Certain short peptides, which are able to translocate across cell membranes with a low lytic activity, can be useful as carriers (vectors) for hydrophilic molecules. We have studied three such cell penetrating peptides: pAntp ('penetratin'), pIsl and transportan. pAntp and pIsl originate from the third helix of homeodomain proteins (%%%Antennapedia%%% and Isl-1, respectively). Transportan is a synthetic %%%chimera%%% (galanin and mastoparan). The peptides in the presence of various phospholipid vesicles (neutral and charged) and SDS micelles have been characterized by spectroscopic methods (fluorescence, EPR and CD). The dynamics of pAntp were monitored using an N-terminal spin label. In aqueous solution, the CD spectra of the three peptides show secondary structures dominated by random coil. With phospholipid vesicles, neutral as well as negatively charged, transportan gives up to 60% alpha-helix. pAntp and pIsl bind significantly only to negatively charged vesicles with an induction of around 60% beta-sheet-like secondary structure. With all three peptides, SDS micelles stabilize a high degree of alpha-helical structure. We conclude that the exact nature of any secondary structure induced by the membrane model systems is not directly correlated with the common transport property of these translocating peptides.

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DIALOG(R)File 5:Biosis Previews(R)

15909514 BIOSIS NO.: 200100081353
Highly specific, membrane-permeant peptide blockers of cGMP-dependent protein kinase Ialpha inhibit NO-induced cerebral dilation
AUTHOR: Dostmann Wolfgang R G (Reprint); Taylor Mark S; Nickl Christian K; Brayden Joseph E; Frank Ronald; Tegge Werner J
AUTHOR ADDRESS: Department of Pharmacology, Department of Molecular Physiology and Biophysics, College of Medicine, University of Vermont, Burlington, VT, 05405-0068, USA**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 97 (26): p14772-14777 December 19, 2000 2000
MEDIUM: print
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Arrays of octameric peptide libraries on cellulose paper were screened by using 32P-autophosphorylated cGMP-dependent protein kinase Ialpha (cGPK) to identify peptide sequences with high binding affinity for cGPK. Iterative deconvolution of every amino acid position in the peptides identified the sequence LRK5H (W45) as having the highest binding affinity. Binding of W45 to cGPK resulted in selective inhibition of the kinase with Ki values of 0.8 muM and 560 muM for cGPK and cAMP-dependent protein kinase (cAPK), respectively. %%%Fusion%%% of W45 to membrane translocation signals from HIV-1 tat protein (YGRKKRRQRRRPP-LRK5H, DT-2) or Drosophila %%%Antennapedia%%% homeo-domain (RQIKIWFQNRRMKWKK-LRK5H, DT-3) proved to be an efficient method for intracellular delivery of these highly charged peptides. Rapid translocation of the peptides into intact cerebral arteries was demonstrated by using fluorescein-labeled DT-2 and DT-3. The inhibitory potency of the %%%fusion%%% peptides was even greater than that for W45, with Ki values of 12.5 nM and 25 nM for DT-2 and DT-3, respectively. Both peptides were still poor inhibitors of cAPK. Selective inhibition of cGPK by DT-2 or DT-3 in the presence of cAPK was demonstrated in vitro. In pressurized cerebral arteries, DT-2 and DT-3 substantially decreased NO-induced dilation. This study provides functional characterization of a class of selective cGPK inhibitor peptides in vascular smooth muscle and reveals a central role for cGPK in the modulation of vascular contractility.

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DIALOG(R)File 5:Biosis Previews(R)

15828082 BIOSIS NO.: 200000546395
Inhibition of pancreatic cancer growth by %%%antennapedia%%%-p16INK4A %%%fusion%%% peptide
AUTHOR: Hosotani R (Reprint); Miyamoto Y (Reprint); Fujimoto K (Reprint); Wada M (Reprint); Doi R (Reprint); Imamura M (Reprint)
AUTHOR ADDRESS: Dept. Surg. and Surgical Basic Sci., Kyoto Univ., Kyoto, Japan**Japan
JOURNAL: Pancreas 21 (4): p448 November, 2000 2000
MEDIUM: print
CONFERENCE/MEETING: The Joint Meeting of the American Pancreatic Association and International Association of Pancreatology Chicago, Illinois, USA November 01-05, 2000; 20001101
ISSN: 0885-3177
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RECORD TYPE: Citation
LANGUAGE: English

1/7/23
DIALOG(R)File 5:Biosis Previews(R)

15783696 BIOSIS NO.: 200000502009
Inhibition of pRb phosphorylation and cell cycle progression by an %%%antennapedia%%%-p16INK4A %%%fusion%%% peptide in pancreatic cancer cells

AUTHOR: Fujimoto Koji (Reprint); Hosotani Ryo; Miyamoto Yoshiharu; Doi Ryuichiro; Koshiba Takatomo; Otaka Akira; Fujii Nobutaka; Beauchamp Robert D; Imamura Masayuki
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JOURNAL: Cancer Letters 159 (2): p151-158 October 31, 2000 2000
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LANGUAGE: English

ABSTRACT: In this study, we examined whether or not a small peptide derived from p16INK4A protein with the %%%antennapedia%%% carrier sequence could inhibit the growth of pancreatic cancer cells through the inhibition of cell progression. Growth inhibition by the p16-derived peptide was observed in a time-and dose-dependent manner in AsPC-1 and BxPC-3 cells (p16-negative and pRb-positive), whereas Saos-2 cells (p16-positive and pRb-negative) showed no inhibitory effect. In AsPC-1 and BxPC-3 cells, the proportion of cells in the G1 phase markedly increased 48 h after treatment with 20 muM p16-derived peptide. Cell-cycle analysis of Saos-2 cells showed little change during the entire period of treatment. Immunoblot analysis showed inhibition of pRb phosphorylation after treatment of BxPC-3 with 10 muM p16 peptide. Furthermore, the p16 peptide caused a decrease in cyclin A at later times of treatment. These results demonstrate that the p16-derived peptide can inhibit the growth of p16-negative and pRb-positive pancreatic cancer cells by means of G1 phase cell cycle arrest from the inhibition of pRb phosphorylation. Restoration of p16/pRb tumor-suppressive pathway by re-expression of p16INK4A may play a therapeutic role in the treatment of pancreatic cancer.

1/7/24
DIALOG(R)File 5:Biosis Previews(R)

15577973 BIOSIS NO.: 200000296286
Inhibition of telomerase activity by a cell-penetrating peptide nucleic acid construct in human melanoma cells
AUTHOR: Villa Raffaella; Folini Marco; Lualdi Susanna; Veronese Silvio; Daidone Maria Grazia; Zaffaroni Nadia (Reprint)
AUTHOR ADDRESS: Department of Experimental Oncology, National Cancer Institute, Via Venezian 1, Unit No. 10, 20133, Milan, Italy**Italy
JOURNAL: FEBS Letters 473 (2): p241-248 May 12, 2000 2000
MEDIUM: print
ISSN: 0014-5793
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RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We investigated the effect of two peptide nucleic acids (PNAs), which are complementary to the RNA component of human telomerase, on the catalytic activity of the enzyme. PNAs induced a dose-dependent reduction of telomerase activity in cell extracts from human melanoma cell lines and surgical specimens. To down-regulate telomerase in intact cells, we generated a %%%chimeric%%% molecule synthesized by coupling the 13-mer

PNA to the %%%Antennapedia%%% peptide. The PNA construct induced a dose- and time-dependent inhibition of telomerase activity. However, a 20-day exposure to the PNA construct only caused a slight increase in melanoma cell doubling time and failed to induce any telomere shortening.

1/7/25
DIALOG(R)File 5:Biosis Previews(R)

15386082 BIOSIS NO.: 200000104395
PSM, a mediator of PDGF-BB-, IGF-I-, and insulin-stimulated mitogenesis
AUTHOR: Riedel Heimo (Reprint); Yousaf Nasim; Zhao Yuyuan; Dai Heping; Deng Youping; Wang Jian
AUTHOR ADDRESS: Department of Biological Sciences, 2171 BSB, Wayne State University, Detroit, MI, 48202-3917, USA**USA
JOURNAL: Oncogene 19 (1): p39-50 Jan. 6, 2000 2000
MEDIUM: print
ISSN: 0950-9232
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: PSM/SH2-B has been described as a cellular partner of the FcepsilonRI receptor, insulin receptor (IR), insulin-like growth factor-I (IGF-I) receptor (IGF-IR), and nerve growth factor receptor (TrkA). A function has been proposed in neuronal differentiation and development but its role in other signaling pathways is still unclear. To further elucidate the physiologic role of PSM we have identified additional mitogenic receptor tyrosine kinases as putative PSM partners including platelet-derived growth factor (PDGF) receptor (PDGFR) beta, hepatocyte growth factor receptor (Met), and fibroblast growth factor receptor. We have mapped Y740 as a site of PDGFR beta that is involved in the association with PSM. We have further investigated the putative role of PSM in mitogenesis with three independent experimental strategies and found that all consistently suggested a role as a positive, stimulatory signaling adapter in normal NIH3T3 and baby hamster kidney fibroblasts. (1) PSM expression from cDNA using an ecdysone-regulated transient expression system stimulated PDGF-BB-, IGF-I-, and insulin- but not EGF-induced DNA synthesis in an ecdysone dose-responsive fashion; (2) Microinjection of the (dominant negative) PSM SH2 domain interfered with PDGF-BB- and insulin-induced DNA synthesis; and (3) A peptide mimetic of the PSM Pro-rich putative SH3 domain-binding region interfered with PDGF-BB-, IGF-I-, and insulin- but not with EGF-induced DNA synthesis in NIH3T3 fibroblasts. This experiment was based on cell-permeable %%%fusion%%% peptides with the Drosophila %%%antennapedia%%% homeodomain which effectively traverse the plasma membrane of cultured cells. These experimental strategies independently suggest that PSM functions as a positive, stimulatory, mitogenic signaling mediator in PDGF-BB, IGF-I, and insulin but not in EGF action. This function appears to involve the PSM SH2 domain as well as the Pro-rich putative SH3 domain binding region. Our findings support the model that PSM participates as an adapter in various mitogenic signaling mechanisms by linking an activated (receptor) phospho-tyrosine to the SH3 domain of an unknown cellular partner.

1/7/26
DIALOG(R)File 5:Biosis Previews(R)

15171757 BIOSIS NO.: 199900431417
Grb10, a positive, stimulatory signaling adapter in platelet-derived growth factor BB-, insulin-like growth factor I-, and insulin-mediated mitogenesis
AUTHOR: Wang Jian; Dai Heping; Yousaf Nasim; Moussaif Mustapha; Deng Youping; Boufelliga Amale; Swamy O Rama; Leone Michelle E; Riedel Heimo (Reprint)
AUTHOR ADDRESS: Department of Biological Sciences, Wayne State University, 2171 BSB, Detroit, MI, 48202-3917, USA**USA
JOURNAL: Molecular and Cellular Biology 19 (9): p6217-6228 Sept., 1999
1999
MEDIUM: print
ISSN: 0270-7306
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Grb10 has been described as a cellular partner of several receptor tyrosine kinases, including the insulin receptor (IR) and the insulin-like growth factor I (IGF-I) receptor (IGF-IR). Its cellular role is still unclear and a positive as well as an inhibitory role in mitogenesis depending on the cell context has been implicated. We have tested other mitogenic receptor tyrosine kinases as putative Grb10 partners and have identified the activated forms of platelet-derived growth factor (PDGF) receptor beta (PDGFRbeta), hepatocyte growth factor receptor (Met), and fibroblast growth factor receptor as candidates. We have mapped Y771 as a PDFGRbeta site that is involved in the association with Grb10 via its SH2 domain. We have further investigated the putative role of Grb10 in mitogenesis with four independent experimental strategies and found that all consistently suggested a role as a positive, stimulatory signaling adaptor in normal fibroblasts. (i) Complete Grb10 expression from cDNA with anecdysone-regulated transient expression system stimulated PDGF-BB-, IGF-I, and insulin- but not epidermal growth factor (EGF)-induced DNA synthesis in an ecdysone dose-responsive fashion. (ii) Microinjection of the (dominant-negative) Grb10 SH2 domain interfered with PDGF-BB- and insulin-induced DNA synthesis. (iii) Alternative experiments were based on cell-permeable %%%fusion%%% peptides with the Drosophila %%%antennapedia%%% homeodomain which effectively traverse the plasma membrane of cultured cells. A cell-permeable Grb10 SH2 domain similarly interfered with PDGF-BB-, IGF-I-, and insulin-induced DNA synthesis. In contrast, a cell-permeable Grb10 Pro-rich putative SH3 domain binding region interfered with IGF-I- and insulin- but not with PDGF-BB- or EGF-induced DNA synthesis. (iv) Transient overexpression of complete Grb10 increased whereas cell-permeable Grb10 SH2 domain %%%fusion%%% peptides substantially decreased the cell proliferation rate (as measured by cell numbers) in normal fibroblasts. These experimental strategies independently suggest that Grb10 functions as a positive, stimulatory, mitogenic signaling adapter in PDGF-BB, IGF-I, and insulin action. This function appears to involve the Grb10 SH2 domain, a novel sequence termed BPS, and the Pro-rich putative SH3 domain binding region in IGF-I- and insulin-mediated mitogenesis. In contrast, PDGF-BB-mediated mitogenesis appears to depend on the SH2 but not on the Pro-rich region and may

involve other, unidentified Grb10 domains. Distinct protein domains may help to define specific Grb10 functions in different signaling pathways.

1/7/27
DIALOG(R)File 5:Biosis Previews(R)

15028294 BIOSIS NO.: 199900287954
Inhibition of pRB phosphorylation and cell cycle progression by an %%%Antennapedia%%%-p16INK4A %%%fusion%%% peptide in pancreatic cancer cells
AUTHOR: Fujimoto Koji (Reprint); Hosotani Ryo (Reprint); Doi Ryuichiro (Reprint); Koshiba Takatomo (Reprint); Miyamoto Yoshiharu (Reprint); Ida Jun (Reprint); Tsuji Shoichiro (Reprint); Kawaguchi Michiya (Reprint); Nakajima Sanae (Reprint); Kobayashi Hiroyuki (Reprint); Imamura Masayuki (Reprint)
AUTHOR ADDRESS: Kyoto Univ, Kyoto, Japan**Japan
JOURNAL: Gastroenterology 116 (4 PART 2): pA407 April, 1999 1999
MEDIUM: print
CONFERENCE/MEETING: Digestive Disease Week and the 100th Annual Meeting of the American Gastroenterological Association Orlando, Florida, USA May 16-19, 1999; 19990516
SPONSOR: American Gastroenterological Association
ISSN: 0016-5085
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

1/7/28
DIALOG(R)File 5:Biosis Previews(R)

14989068 BIOSIS NO.: 199900248728
Bak BH3 peptides antagonize Bcl-xL function and induce apoptosis through cytochrome c-independent activation of caspases
AUTHOR: Holinger Eric P; Chittenden Thomas; Lutz Robert J (Reprint)
AUTHOR ADDRESS: Apoptosis Technology, Inc., 148 Sidney St., Cambridge, MA, 02139, USA**USA
JOURNAL: Journal of Biological Chemistry 274 (19): p13298-13304 May 7, 1999 1999
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The Bcl-2 homology 3 (BH3) domain is crucial for the death-inducing and dimerization properties of pro-apoptotic members of the Bcl-2 protein family, including Bak, Bax, and Bad. Here we report that synthetic peptides corresponding to the BH3 domain of Bak bind to Bcl-xL, antagonize its anti-apoptotic function, and rapidly induce apoptosis when delivered into intact cells via %%%fusion%%% to the %%%Antennapedia%%% homeoprotein internalization domain. Treatment of HeLa cells with the %%%Antennapedia%%%-BH3 %%%fusion%%% peptide resulted in peptide internalization and induction of apoptosis within 2-3 h, as

indicated by caspase activation and subsequent poly-(ADP-ribose) polymerase cleavage, as well as morphological characteristics of apoptosis. A point mutation within the BH3 peptide that blocks its ability to bind to Bcl-xL abolished its apoptotic activity, suggesting that interaction of the BH3 peptide with Bcl-2-related death suppressors, such as Bcl-xL, may be critical for its activity in cells. While overexpression of Bcl-xL can block BH3-induced apoptosis, treatment with BH3 peptides resensitized Bcl-xL-expressing cells to Fas-mediated apoptosis. BH3-induced apoptosis was blocked by caspase inhibitors, demonstrating a dependence on caspase activation, but was not accompanied by a dramatic early loss of mitochondrial membrane potential or detectable translocation of cytochrome c from mitochondria to cytosol. These findings demonstrate that the BH3 domain itself is capable of inducing apoptosis in whole cells, possibly by antagonizing the function of Bcl-2-related death suppressors.

1/7/29
DIALOG(R)File 5:Biosis Previews(R)

14612916 BIOSIS NO.: 199800407163
Inhibition of cancer cell growth and c-Myc transcriptional activity by a c-Myc helix 1-type peptide fused to an internalization sequence
AUTHOR: Giorello Laura; Clerico Luana; Pescarolo Maria Pia; Vikhanskaya Faina; Salmona Mario; Colella Gennaro; Bruno Silvia; Mancuso Tommaso; Bagnasco Luca; Russo Patrizia; Parodi Silvio (Reprint)
AUTHOR ADDRESS: Dep. Exp. Oncol., Ist. Nazionale per la Ricerca sul Cancro, Largo R. Benzi 10, Genoa 16132, Italy**Italy
JOURNAL: Cancer Research 58 (16): p3654-3659 Aug. 15, 1998 1998
MEDIUM: print
ISSN: 0008-5472
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: c-Myc is a nuclear protein with important roles in cell transformation, cell proliferation, and gene transcription. It has been previously shown that a 14-amino acid (aa) modified peptide (H1-S6A,F8A) derived from the helix 1 (H1) carboxylic region of c-Myc can interfere in vitro with specific c-Myc DNA binding. Here, we have linked the above Myc-derived 14-aa peptide to a 16-aa sequence from the third helix of %%%Antennapedia%%% (Int). It has been repeatedly reported that this 16-aa %%%Antennapedia%%% peptide is able to cross mammalian cell membranes and to work as a vector for short peptides. Using fluorescent (dansylated or rhodaminated) peptides, we have shown that the %%%fusion%%% peptide with the %%%Antennapedia%%% fragment (Int-H1S6A,F8A) but not the c-Myc derived fragment alone (H1-S6A,F8A) was capable of internalization inside MCF-7 human breast cancer cells. Int-H1-S6A,F8A and H1-S6A,F8A were the only two peptides capable of inhibiting coimmunoprecipitation of the c-Myc/Max heterodimer in vitro. We have treated (continuously for 10-11 days) MCF-7 cells with four different peptides: Int, H1-S6A,F8A, Int-H1-S6A,F8A, and Int-H1wt (a peptide differing from Int-H1-S6A,F8A by 2 aa (S6 and F8) in the H1 region). In intact MCF-7 cells, Int-H1-S6A,F8A was the only active peptide capable of inducing the following biological effects: (a) inhibition of cloning efficiency on plates; (b) inhibition of cell growth and induction of apoptosis in subconfluent/confluent cells; and (c)

inhibition of transcription of two c-Myc-regulated genes (ODC and p53). Int-H1-S6A,F8A was active in the 1-10 muM range. Int-H1-S6A,F8A may represent a lead molecule for peptidomimetic compounds that have a similar three-dimensional structure but are more resistant to peptidases and, therefore, suitable for in vivo treatment of experimentally induced tumors.

1/7/30
DIALOG(R)File 5:Biosis Previews(R)

14474302 BIOSIS NO.: 199800268549
Features of replicative senescence induced by direct addition of %%%antennapedia%%%-p16INK4A %%%fusion%%% protein to human diploid fibroblasts
AUTHOR: Kato Daishiro; Miyazawa Kazuhiro; Ruas Marugarida; Starborg Maria; Wada Ikuo; Oka Takahiro; Sakai Toshiyuki; Peters Gordon; Hara Eiji (Reprint)
AUTHOR ADDRESS: Dep. Preventive Med., Kyoto Prefectural Univ. Med., Kawaramachi-Hirokoji, Kamigyo-ku, Kyoto 602-0841, Japan**Japan
JOURNAL: FEBS Letters 427 (2): p203-208 May 8, 1998 1998
MEDIUM: print
ISSN: 0014-5793
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The p16INK4A cyclin-dependent kinase (Cdk) inhibitor is now recognized as a major tumor suppressor that is inactivated by a variety of mechanisms in a wide range of human cancers. It is also implicated in the mechanisms underlying replicative senescence since p16INK4A RNA and protein accumulate as cells approach their proscribed limit of population doublings in tissue culture. To obtain further evidence of its role in senescence, we have sought ways of overexpressing p16INK4A in primary human diploid fibroblasts (HDF). To circumvent the low transfection efficiency of primary cells we have exploited a recombinant form of the full-length p16INK4A protein fused to a 16 amino acid peptide from the Drosophila %%%antennapedia%%% protein. This peptide has the capacity to cross both cytoplasmic and nuclear membranes allowing the direct introduction of the active protein to primary cells. Here, we show that %%%antennapedia%%%-tagged wild-type p16INK4A protein, but not a functionally compromised tumor-specific variant, causes GI arrest in early passage HDFs by inhibiting the phosphorylation of the retinoblastoma protein. Significantly, the arrested cells display several phenotypic features that are considered characteristic of senescent cells. These data support a role for p16INK4A in replicative senescence and raise the possibility of using the %%%antennapedia%%%-tagged protein therapeutically.

1/7/31
DIALOG(R)File 5:Biosis Previews(R)

14324223 BIOSIS NO.: 199800118470
Interaction between spineless-aristapedia gene and genes from

%%%Antennapedia%%% and bithorax complexes of Drosophila melanogaster
AUTHOR: Kuzin Boris (Reprint); Doszhanov Kuanysh; Mazo Alexander
AUTHOR ADDRESS: Kol'tsov Inst. Developmental Biol., Russian Acad. Sci., Vavilov Street 26, Moscow, 117808, Russia**Russia
JOURNAL: International Journal of Developmental Biology 41 (6): p867-875 Dec., 1997 1997
MEDIUM: print
ISSN: 0214-6282
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Mutations in the spineless-aristapedia (ssa) gene of Drosophila melanogaster are pleiotropic, and their classical manifestations include a reduction in size of all bristles (spineless phenotype), transformation of distal parts of antennae into tarsal segments of the mesothoracic leg (aristapedia phenotype), and, in extreme alleles, %%%fusion%%% of tarsal segments on all six legs and the transformed aristaes. We isolated a new allele, which is a severe loss-of-function mutation and, in addition to the above-mentioned features, is characterized by amplification of sex combs on the first leg. This phenotype can be caused by a change in the expression of the Sex combs reduced (Scr) gene of the ANTP-C. Identification of this phenotype, together with observed variations in the extent of the %%%fusion%%% of tarsal segments in the legs of different segments, raised the possibility that ssa interacts with homeotic genes controlling the identity of segments. This possibility was tested in genetical experiments using flies with loss-of-function mutations in several homeotic genes and flies transformed by heat shock-driven homeotic genes. Analysis of.adult phenotypes of different ssa alleles in the background of under-, over-, or ectopic expression of some genes of BX-C and ANTC suggests that the se product is required to prevent the effect of the homeotic gene products in the distal segments of the appendages.

1/7/32
DIALOG(R)File 5:Biosis Previews(R)

14276676 BIOSIS NO.: 199800070923
Synthesis and membrane permeability of PNA-peptide conjugates
AUTHOR: Simmons Carla G; Pitts Anne E; Mayfield Lynn D; Shay Jerry W; Corey David R (Reprint)
AUTHOR ADDRESS: Dep. Pharmacol., Howard Hughes Med. Inst., 5323 Harry Hines Blvd., Dallas, TX 75235, USA**USA
JOURNAL: Bioorganic and Medicinal Chemistry Letters 7 (23): p3001-3006 Dec. 2, 1997 1997
MEDIUM: print
ISSN: 0960-894X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: %%%Chimeric%%% molecules consisting of peptide nucleic acid oligomers (PNAs) and peptides derived from the third helix of the homeodomain of %%%Antennapedia%%% are taken up by mammalian cells in culture. Uptake is independent of orientation and occurs with high

efficiency, suggesting that peptide conjugates are a promising strategy for intracellular PNA delivery.

1/7/33
DIALOG(R)File 5:Biosis Previews(R)

14019350 BIOSIS NO.: 199799653410
Nuclear punctate distribution of ALL-1 is conferred by distinct elements at the N terminus of the protein
AUTHOR: Yano Takahiro; Nakamura Tatsuya; Blechman Janna; Sorio Claudio; Dang Chi V; Geiger Benjamin; Canaani Eli (Reprint)
AUTHOR ADDRESS: Dep. Mol. Cell Biol., Weizmann Inst. Sci., Rehovot 76100, Israel**Israel
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 94 (14): p7286-7291 1997 1997
ISSN: 0027-8424
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The ALL-1 gene positioned at 11q23 is directly involved in human acute leukemia either through a variety of chromosome translocations or by partial tandem duplications. ALL-1 is the human homologue of Drosophila trithorax which plays a critical role in maintaining proper spatial and temporal expression of the %%%Antennapedia%%%-bithorax homeotic genes determining the fruit fly's body pattern. Utilizing specific antibodies, we found that the ALL-1 protein distributes in cultured cells in a nuclear punctate pattern. Several %%%chimeric%%% ALL-1 proteins encoded by products of the chromosome translocations and expressed in transfected cells showed similar speckles. Dissection of the ALL-1 protein identified within its -1,100 N-terminal residues three polypeptides directing nuclear localization and at least two main domains conferring distribution in dots. The latter spanned two short sequences conserved with TRITHORAX. Enforced nuclear expression of other domains of ALL-1, such as the PHD (zinc) fingers and the SET motif, resulted in uniform nonpunctate patterns. This indicates that positioning of the ALL-1 protein in subnuclear structures is mediated via interactions of ALL-1 N-terminal elements. We suggest that the speckles represent protein complexes which contain multiple copies of the ALL-1 protein and are positioned at ALL-1 target sites on the chromatin. Therefore, the role of the N-terminal portion of ALL-1 is to direct the protein to its target genes.

1/7/34
DIALOG(R)File 5:Biosis Previews(R)

13986482 BIOSIS NO.: 199799620542
A truncated HIV-1 Tat protein basic domain rapidly translocates through the plasma membrane and accumulates in the cell nucleus
AUTHOR: Vives Eric; Brodin Priscille; Lebleu Bernard (Reprint)
AUTHOR ADDRESS: Institut de Genetique Moleculaire de Montpellier, CNRS-UMR 5535, BP5051, 1919 route de Mende, 34033 Montpellier cedex 1, France** France

JOURNAL: Journal of Biological Chemistry 272 (25): p16010-16017 1997 1997
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Tat is an 86-amino acid protein involved in the replication of human immunodeficiency virus type 1 (HIV-1). Several studies have shown that exogenous Tat protein was able to translocate through the plasma membrane and to reach the nucleus to transactivate the viral genome. A region of the Tat protein centered on a cluster of basic amino acids has been assigned to this translocation activity. Recent data have demonstrated that chemical coupling of a Tat-derived peptide (extending from residues 37 to 72) to several proteins allowed their functional internalization into several cell lines or tissues. A part of this same domain can be folded in an a-helix structure with amphipathic characteristics. Such helical structures have been considered as key determinants for the uptake of several enveloped viruses by %%%fusion%%% or endocytosis. In the present study, we have delineated the main determinants required for Tat translocation within this sequence by synthesizing several peptides covering the Tat domain from residues 37 to 60. Unexpectedly, the domain extending from amino acid 37 to 47, which corresponds to the alpha-helix structure, is not required for cellular uptake and for nuclear translocation. Peptide internalization was assessed by direct labeling with fluorescein or by indirect immunofluorescence using a monoclonal antibody directed against the Tat basic cluster. Both approaches established that all peptides containing the basic domain are taken up by cells within less than 5 min at concentrations as low as 100 nM. In contrast, a peptide with a full alpha-helix but with a truncated basic amino acid cluster is not taken up by cells. The internalization process does not involve an endocytic pathway, as no inhibition of the uptake was observed at 4 degree C. Similar observations have been reported for a basic amino acid-rich peptide derived from the %%%Antennapedia%%% homeodomain (1). Short peptides allowing efficient translocation through the plasma membrane could be useful vectors for the intracellular delivery of various non-permeant drugs including antisense oligonucleotides and peptides of pharmacological interest.

1/7/35
DIALOG(R)File 5:Biosis Previews(R)

13684035 BIOSIS NO.: 199799318095
ALL-1 interacts with unr, a protein containing multiple cold shock domains
AUTHOR: Leshkowitz D; Rozenblatt O; Nakamura T; Yano T; Dautry F; Croce C M ; Canaani E (Reprint)
AUTHOR ADDRESS: Dep. Mol. Cell Biol., Weizmann Inst. Sci., Rehovot 76100, Israel**Israel
JOURNAL: Oncogene 13 (9): p2027-2031 1996 1996
ISSN: 0950-9232
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The ALL-1 gene is involved in human acute leukemia through

chromosome translocations and %%%fusion%%% to partner genes, or through partial tandem duplications. ALL-1 is the human homologue of Drosophila trithorax which transregulates the homeotic genes of the %%%Antennapedia%%% and bithorax complexes controlling body segment identity. ALL-1 encodes a very large protein of 3968 amino acids which presumably interacts with many proteins. Here we applied yeast two hybrid screening to identify proteins interacting with the N-terminal segment of ALL-1. One protein obtained in this way was the product of the unr gene. This protein consists of multiple repeats homologous to the cold shock domain (CSD), a motif common to some bacterial and eukaryotic nucleic acids-binding proteins. The minimal region on unr required for the interaction with ALL-1 included two CSD and two intervening polypeptides. The interaction was confirmed by in vitro binding studies, and by coimmunoprecipitation from COS cells overexpressing the relevant segments of the two proteins. These results suggest that unr is involved in an interaction of ALL-1 with DNA or RNA.

1/7/36
DIALOG(R)File 5:Biosis Previews(R)

13469558 BIOSIS NO.: 199699103618
Introduction of exogenous antigens into the MHC class I processing and presentation pathway by Drosophila %%%antennapedia%%% homeodomain primes cytotoxic T cells in vivo
AUTHOR: Schutze-Redelmeier Marie-Paule; Gournier Helene (Reprint); Garcia-Pons Francois; Moussa Marlene; Joliot Alain J; Volovitch Michel; Prochiantz Alain; Lemonnier Francois A
AUTHOR ADDRESS: Unite d'Immunite Cellulaire Antivirale, Dep. SIDA-Retrovirus, Inst. Pasteur, 28 rue du Dr. Roux, 75724 Paris Cedex 15, France**France
JOURNAL: Journal of Immunology 157 (2): p650-655 1996 1996
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The homeodomain of the %%%Antennapedia%%% molecule (AntpHD) spontaneously crosses cellular membranes and can be used to deliver up to So additional amino acids to the cytoplasm. We exploited this approach to deliver antigenic peptides to the MHC class I processing and presentation pathway. AntpHD-based %%%fusion%%% peptides expressing the 170-179 HLA-Cw3 CTL epitope (pCw3) were produced in bacteria. Incubation of these %%%fusion%%% peptides with H-2-d target cells resulted in efficient delivery to the cytosol as indicated by protease resistance and confocal microscopy. Moreover, this introduction of an exogenous Ag resulted in sensitization of the cell to lysis by a CTL clone specific for the 170-179 HLA-Cw3-derived peptide. Sensitivity of the Ag processing to brefeldin A but not to chloroquine is consistent with the delivery of AntpHD %%%fusion%%% peptides to the conventional class I-associated processing pathway. Immunization of DBA/2 (H-2-d) mice with AntpHD pCw3 %%%fusion%%% peptide in the presence of SDS primed H-2K-d-restricted HLA-Cw3-specific CTL. Similar results were obtained with AntpHD %%%fusion%%% peptides expressing the 147-156 influenza nucleoprotein peptide. The strategy outlined in this paper provides a new approach for introducing molecules into the MHC class I Ag-presenting pathway. This

approach has clear relevance to the design of synthetic peptide-based vaccines.

1/7/37
DIALOG(R)File 5:Biosis Previews(R)

13164358 BIOSIS NO.: 199698632191
Sequence and expression of grasshopper %%%antennapedia%%%: Comparison to Drosophila
AUTHOR: Hayward David C (Reprint); Patel Nipam H; Rehm E Jay; Goodman Corey S; Ball Eldon E
AUTHOR ADDRESS: Molecular Evolution and Systematics Group, Res. Sch. Biol. Sci., Aust. Natl. Univ., P.O. Box 475, Canberra, ACT 2601, Australia** Australia
JOURNAL: Developmental Biology 172 (2): p452-465 1995 1995
ISSN: 0012-1606
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have cloned and characterized the %%%Antennapedia%%% (Antp) gene from the grasshopper Schistocerca americana. The %%%Antennapedia%%% protein contains seven blocks of sequence, including the homeodomain, that are conserved in the homologous proteins of other insects, interspersed with (usually repetitive) sequences unique to each species. There is no similarity between 1.8 kb of 3' untranslated sequence in grasshopper and Drosophila. We examined %%%Antennapedia%%% protein expression in grasshopper using an antibody raised against a grasshopper %%%fusion%%% protein and reexamined its expression in Drosophila using several different antibodies. Early patterns of expression in the two insects are quite different, reflecting differing modes of early development. However, by the germband stage, expression patterns are quite similar, with relatively uniform epithelial expression throughout the thoracic and abdominal segments which later retracts to the thorax. Expression is observed in muscle pioneers, the peripheral nervous system, and the central nervous system (CNS). In the CNS expression is initially limited to a few neurons, but eventually becomes widespread. Both insects show strong expression in certain homologous identified neurons and similar temporal modulation of expression.

1/7/38
DIALOG(R)File 5:Biosis Previews(R)

12799217 BIOSIS NO.: 199598267050
Pbx proteins display hexapeptide-dependent cooperative DNA binding with a subset of Hox proteins
AUTHOR: Chang Ching-Pin; Shen Wei-Fang; Rozenfeld Sofia; Lawrence H Jeffrey ; Largman Corey; Cleary Michael L (Reprint)
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ABSTRACT: The human proto-oncogene PBX1 codes for a homolog of Drosophila extradenticle, a divergent homeo domain protein that modulates the developmental and DNA-binding specificity of select HOM proteins. We demonstrate that wild-type Pbx proteins and %%%chimeric%%% E2a-Pbx1 oncoproteins cooperatively bind a consensus DNA probe with HoxB4, B6, and B7 of the %%%Antennapedia%%% class of Hox/HOM proteins. Specificity of Hox-Pbx interactions was suggested by the inability of Pbx proteins to cooperatively bind the synthetic DNA target with HoxA10 or Drosophila even-skipped. Site-directed mutagenesis showed that the hexapeptide motif (IYPWMK) upstream of the Hox homeo domain was essential for HoxB6 and B7 to cooperatively bind DNA with Pbx proteins. Engraftment of the HoxB7 hexapeptide onto HoxA10 endowed it with robust cooperative properties, demonstrating a functional role for the highly conserved hexapeptide element as one of the molecular determinants delimiting Hox-Pbx cooperativity. The Pbx homeo domain was necessary but not sufficient for cooperativity, which required conserved amino acids carboxy-terminal of the homeo domain. These findings demonstrate that interactions between Hox and Pbx proteins modulate their DNA-binding properties, suggesting that Pbx and Hox proteins act in parallel as heterotypic complexes to regulate expression of specific subordinate genes.

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DIALOG(R)File 5:Biosis Previews(R)

12719696 BIOSIS NO.: 199598187529
Levels of homeotic protein function can determine developmental identity: Evidence from low-level expression of the Drosophila homeotic gene proboscipedia under Hsp70 control
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ABSTRACT: The autonomous selector capacity of the homeotic proboscipedia (pb) gene of the Drosophila %%%Antennapedia%%% Complex was tested. We introduced into the germline a P element containing a transcriptional %%%fusion%%% of a mini-gene for pb (normally required for formation of the labial and maxillary palps of the mouthparts) and the Hsp70 promoter. Uninduced expression of this Hsp70-pb element (HSPB) directs a novel, fully penetrant dominant transformation of antennae toward maxillary palps. Gene dosage experiments varying the number of HSPB elements indicate that the extent of the dominant transformation depends on the level of PB protein. At the same time, expression from the transgene also rescues recessive pb mutations. Finally, HSPB function may override the dominant antennal transformations caused by %%%Antennapedia%%% (Antp) mutations in a dose-sensitive manner, directing a switch of the antenna)

disc-derived appendage from ectopic leg to ectopic maxillary palp. This switch correlated with strikingly reduced ANTP protein accumulation when PB concentrations exceeded a genetically defined threshold level. These observations support a crucial role for quantitative aspects of pb function in determining segmental identity, including cross-regulatory events involved in this determination.

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12632750 BIOSIS NO.: 199598100583
The C-terminus of the homeodomain is required for functional specificity of the Drosophila rough gene
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ABSTRACT: In contrast to most Drosophila homeobox genes, which are required during embryogenesis, the rough gene is involved in photoreceptor cell specification in the compound eye. Taking advantage of the viability of null rough alleles and the small size of the rough gene, we have combined in vivo and in vitro mutagenesis to define important functional domains in the rough protein. All missense mutations found to disrupt rough function mapped to highly conserved amino acids in the homeodomain (HD), suggesting that the nature of few, if any, single amino acids outside the HD is critical for rough activity. The analysis of %%%chimeric%%% proteins, in which the whole HD or parts of it were swapped between the rough and %%%Antennapedia%%% (Antp) proteins, revealed that the C-terminus of the rough HD is important for rough activity in vivo. This C-terminal region was also found to be required for the recognition of rough binding sites in vitro. Our data suggest that amino acids located in the C-terminus of the homeodomain may play important roles in selective binding site recognition.
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